VOLUME 59 NUMBER 5

ARCHIVES OF SURGERY

EDITORIAL BOARD

WALTMAN WALTERS, Chairman, Rochester, Minn.
LESTER R. DRAGSTEDT, Chicago
ROBERT ELMAN, St. Louis
ALFRED BLALOCK, Baltimore
ALTON OCHSNER, New Orleans
A. J. SCHOLL, Los Angeles
ARTHUR W. ALLEN, Boston
G. E. LINDSKOG, New Haven, Conn.
COBB PILCHER, Nashville, Tenn.

NOVEMBER 1949

PUBLISHED MONTHLY BY AMERICAN MEDICAL ASSOCIATION, 535 NORTH DEARBORN STREET, CHICAGO 10, ILLINOIS. ANNUAL SUBSCRIPTION, $10.00

Entered as Second Class Matter July 10, 1925, at the Postoffice at Chicago, Under the Act of Congress of March 3, 1879

COPYRIGHT, 1949, BY THE AMERICAN MEDICAL ASSOCIATION

CONTENTS OF PREVIOUS NUMBER

OCTOBER 1949. NUMBER 4

Retrograde Spread of Carcinoma in the Rectum and Rectosigmoid. James F. Connell Jr., M.D., and Antonio Rottino, M.D., New York.

Early and Delayed Clinical Effects of Vagotomy for Peptic Ulcer. Charles S. Kipen, M.D., and G. Arnold Stevens, M.D., Beverly Hills, Calif.

Intravenous Administration of Procaine Hydrochloride for Painful Prolapsed Hemorrhoids. Burnett Schaff, M.D., and J. Gordon Spendlove, M.D., Oteen, N. C.

Treatment of Cancer of Breast by Simple Mastectomy and Roentgenotherapy. Robert McWhirter, F.R.C.S., F.F.R., Edinburgh, Scotland.

Anesthesia in Traumatic Conditions. Francis F. Foldes, M.D., Pittsburgh.

Short Radius. Henry Milch, M.D., New York.

Use of Skin Grafts in Repair of Cleft Palate to Improve Speech. Hamilton Baxter, M.D., D.D.S.; John Drummond, M.D., D.D.S., and Martin Entin, M.D., Montreal, Canada.

Contusions of the Lung from Nonpenetrating Injuries to the Thorax. W. C. Sealy, M.D., Durham, N. C.

Technic for Arthrodesis of the Hip When the Femoral Head and Neck Are Absent. Leon L. Wiltse, M.D., Long Beach, Calif., and Walter A. L. Thompson, M.D., New York.

Relief of Chronic Hypertension by Excision of Pheochromocytoma. Frederick M. Owens Jr., M.D., Chicago.

Drill Perforation, a Simplified Method for Ventricular Puncture. T. C. Erickson, M.D., and H. M. Suckle, M.D., Madison, Wis.

Xanthomatous Giant Cell Tumors Arising in Soft Tissue: Report of an Instance of Malignant Growth. Mathew W. Kobak, M.D., and Samuel Perlow, M.D., Chicago.

Granulomas of Large Size Caused by Implantation of Talcum (Talcum Sarcoids). G. E. Gruenfeld, M.D., St. Louis.

Pseudocyst of the Liver: Report of a Case. Edgar J. Poth, M.D., Ph.D., and A. William DeLoach, M.D., Galveston, Texas.

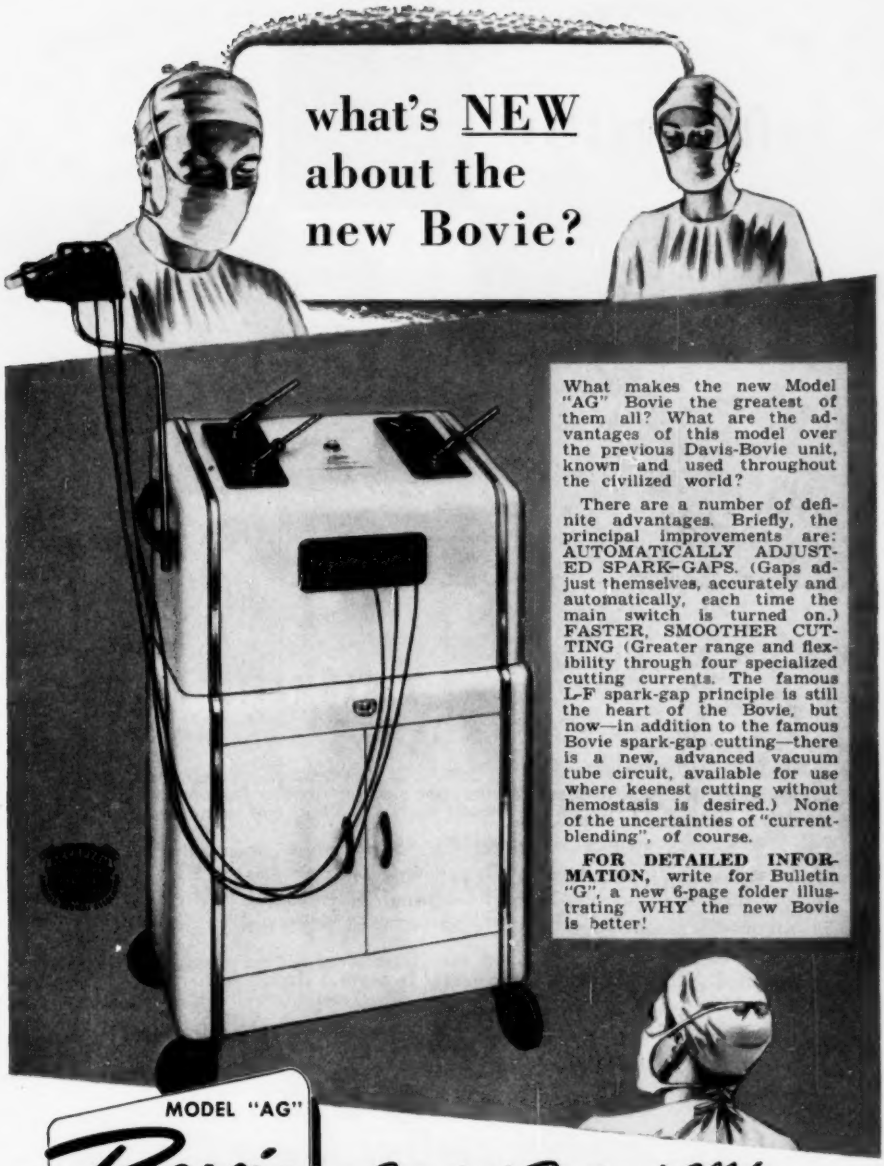
Islet Cell Tumor of the Pancreas. Frederick H. Amendola, M.D., New York.

Granulomas of the Ileocecal Region Secondary to Appendicitis (Ligneous Cecitis) Which Simulate Neoplasms. James W. Wilson, M.D.; Malcolm B. Dockerty, M.D.; John M. Waugh, M.D., and J. Arnold Bargen, M.D., Rochester, Minn.

Progress in Orthopedic Surgery for 1946. A Review Prepared by an Editorial Board of the American Academy of Orthopaedic Surgeons:

XVII. Infantile Paralysis; Research. J. A. Toomey, M.D., Cleveland.

XVIII. Neuromuscular Disorders Exclusive of Poliomyelitis. Winthrop M. Phelps, M.D., Baltimore, and Robert A. Knight, M.D., Memphis, Tenn.



what's NEW about the new Bovie?

What makes the new Model "AG" Bovie the greatest of them all? What are the advantages of this model over the previous Davis-Bovie unit, known and used throughout the civilized world?

There are a number of definite advantages. Briefly, the principal improvements are: AUTOMATICALLY ADJUSTED SPARK-GAPS. (Gaps adjust themselves, accurately and automatically, each time the main switch is turned on.) FASTER, SMOOTHER CUTTING (Greater range and flexibility through four specialized cutting currents. The famous L-F spark-gap principle is still the heart of the Bovie, but now—in addition to the famous Bovie spark-gap cutting—there is a new, advanced vacuum tube circuit, available for use where keenest cutting without hemostasis is desired.) None of the uncertainties of "current-blending", of course.

FOR DETAILED INFORMATION, write for Bulletin "G", a new 6-page folder illustrating WHY the new Bovie is better!

MODEL "AG"

Bovie electrosurgical unit

-Greatest Bovie of All!

LIEBEL-FLARSHEIM

CINCINNATI 2, OHIO

INTRODUCING

All ½-circle
.041" wire diameter

4 NEW DAVIS & GECK ATRAUMATIC® NEEDLES

. . . specially designed to meet requests for smaller needles for obstetrical, intestinal and abdominal closure.

. . . to replace with the Atraumatic principle such needles as Mayo intestinal, regular surgeon's ½-circle, Murphy intestinal, Mayo catgut ½-circle and others in comparable sizes.

. . . supplied with plain or chromic catgut in several sizes.

. . . developed in keeping with D&G's policy of providing a suture-needle combination for every surgical situation.

D & G SUTURES

"This One Thing We Do"

DAVIS & GECK, INC., 57 Willoughby Street, Brooklyn 1, N. Y.

Elimination of preoperative apprehension

Basal anesthesia by the use of Avertin with amylene hydrate, as a simple enema in the patient's own room, eliminates preoperative fear and apprehension. Avertin basal anesthesia spares the patient the ordeal of "sweating it out" during the customary preoperative preparations. Furthermore, it reduces the amount of inhalation anesthetic needed subsequently by about one half and greatly eases the discomfort of the immediate postoperative period.

AVERTIN

with AMYLENE HYDRATE

Avertin, brand of Tribromoethanol

WINTHROP-STEARNS

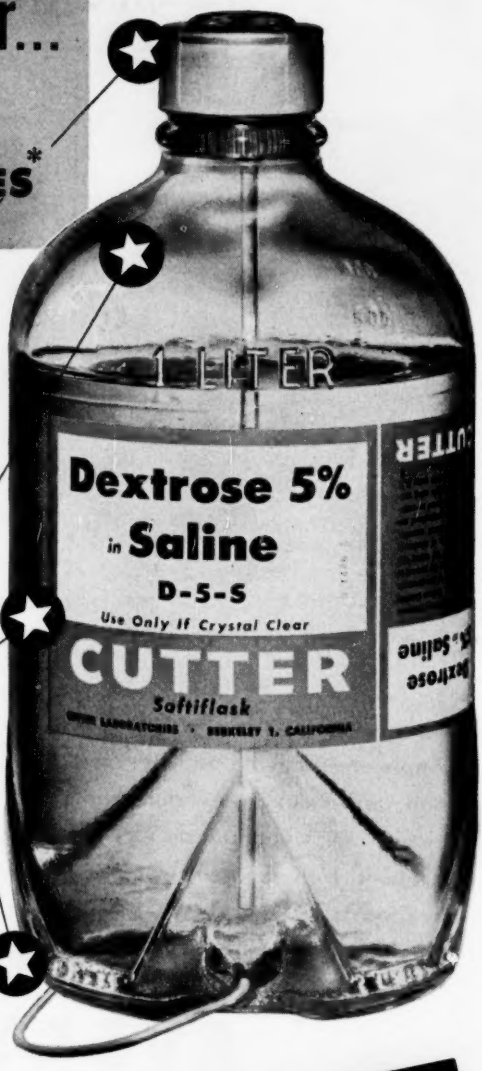
Winthrop-Stearns INC.

NEW YORK 13, N. Y. WINDSOR, ONT.

AVERTIN, trademark reg. U. S. Pat. Off. & Canada

Specify Cutter...

GET *ALL* THESE FEATURES*



SAFTICAP *Look for the gold Saftiseal cap with the large pull-tab. Easy to open—eliminates torn gloves and ripped fingernails.*

BOTTLE *Look for the distinctive shape. Can be stored bottle-to-bottle—requires less storage space.*

LABEL *Look for the easy-to-read Cutter label. Your staff can quickly and accurately check type and percentage of solution. Saves time and eliminates possibility of error.*

BAIL *Look for the safe, new-style bail. Withstands tremendous pressure. The only bail that pops up in place. Permits Saftiflask to be inverted and suspended with one hand.*

You get all these features when you use Cutter Saftiflask Solutions . . . safe, sterile, pyrogen-free, sealed under vacuum and ready for instant use.

Your Cutter Hospital Supplier is at your service with the complete line of Cutter Saftiflask Solutions always available.

CUTTER Saftiflask Solutions

CUTTER LABORATORIES • BERKELEY 10, CALIF.

FOUR NEEDLES DISPLACE 30 NEEDLES

USE THIS CT	USE THIS CT-1	USE THIS CP	USE THIS CP-1
Ethicon Atraloc Large ½ Circle Taper (CT) Med. Chromic Gut 00, 0, 1	Ethicon Atraloc Medium ½ Circle Taper (CT-1) Med. Chromic Gut 000, 00, 0	Ethicon Atraloc Large ½ Circle Cutting (CP) Med. Chromic Gut 00, 0, 1, 2	Ethicon Atraloc Medium ½ Circle Cutting (CP-1) Med. Chromic Gut 000, 00, 0
INSTEAD OF	**INSTEAD OF**	**INSTEAD OF**	**INSTEAD OF**
Mayo Intestinal #1, #2 Murphy Intestinal #1, #2 Ferguson #6, #8 Mayo Catgut #1, #2	Mayo Intestinal #3, #4 Murphy Intestinal #3, #4 Ferguson #10, #12 Mayo Catgut #3, #4	Regular Surgeon's #2, #3 Fistula #2, #3 Mayo Trocar #2 Martin's Uterine #4	Regular Surgeon's #4, #5 Fistula #4, #5 Mayo Trocar #3, #4 Martin's Uterine #5, #6
ONE NEEDLE DISPLACES 8	**ONE NEEDLE DISPLACES 8**	**ONE NEEDLE DISPLACES 6**	**ONE NEEDLE DISPLACES 8**

THESE 30 EYED NEEDLES REPRESENT 80% OF THE NEEDLES USED IN ABDOMINAL CLOSURE

Hospital Expenses Reduced by Needle Standardization

Substantial savings are made when surgical staff personnel standardizes on needles as suggested in the above chart. The eyeless needles are always ready and are easier to use. No unthreading. Operating time reduced.

The hospital reduces its inventory and investment. Nurse time is saved by eliminating preparation and sterilization. There is no need to scrub, polish or sharpen the needles.

ORDER FROM YOUR SURGICAL SUPPLY DISTRIBUTOR

ETHICON *Sutures*

ETHICON SUTURES LABORATORIES, ***Division of Johnson & Johnson,*** **NEW BRUNSWICK, N. J.**

in place of meat

Whenever the nutritional needs of the patient cannot be met with oral feeding or when large volumes of plasma are not available, you cannot choose a safer, more complete source of amino acids than the AMINOSOL line of parenteral solutions.

Aminosol is derived from blood fibrin, a protein of high biologic value. With AMINOSOL as the sole source of protein, good nitrogen retention, plasma protein regeneration, weight gain and protein repletion have been amply demonstrated. AMINOSOL is sterilized both by filtration and by autoclaving and is subjected to rigid antigenicity control. Its potassium, magnesium, calcium and phosphorus content is adequate, its sodium salt content low. (AMINOSOL also available with salt added.) Vitamin B complex and vitamin C may be added to the solutions by simple injection through the rubber tubing after infusion has started.

Ask your Abbott Representative how this safe, convenient, adaptable line can aid your program of protein therapy. For literature, send your card to ABBOTT LABORATORIES, NORTH CHICAGO, ILL.

5% Solution.
5% with Dextrose 5%.
5% with Dextrose 5% and Sodium Chloride 0.3%.

AMINOSOL®

(ABBOTT'S MODIFIED FIBRIN HYDROLYSATE)

ARCHIVES OF SURGERY

VOLUME 59 NOVEMBER 1949 NUMBER 5

COPYRIGHT, 1949, BY THE AMERICAN MEDICAL ASSOCIATION

ACUTE ABDOMINAL MANIFESTATIONS IN SICKLE CELL DISEASE

A Report of Three Cases, with Laparotomy in Two

PHILIP CRASTNOPOL, M.D.

AND

CHARLES F. STEWART, M.D.

NEW YORK

ONLY a small proportion of Negroes with the sickle cell trait have the active form of the disease.[1] In 1929 Levy[2] found that of 213 Negroes admitted in succession to the New Rochelle Hospital, 12, or 5.8 per cent, had "sickling." Murphy and Shapiro[3] recorded its incidence in the North American Negro as from 7 to 13 per cent, with anywhere from 1 in 7 to 1 in 40 of those affected showing clinical disease and with a total of almost 135,000 diseased in the United States. Wintrobe[4] expressed the belief that 1 in 40 Negroes in North America and up to 9 per cent in Central and South America are so affected.

Huck[5] first pointed out that the trait was transmitted by the male and the female as a mendelian dominant characteristic. It occurs in males in a ratio of 3 to 1[6]; usually children and adolescents are affected, though persons up to 78 have shown evidence of the disease. It has been reported in white persons,[4] and in 1 case involving a 19 year old American-born white youth it was followed by laparotomy.[7]

The abdominal manifestations of sickle cell disease are generally recognized to be as much a part of it as the pains in the bones, joints and muscles or the leg ulcers, but their cause remains obscure. The

---

From the Second Surgical Service, Lincoln Hospital.

1. Campbell, E. H.: Acute Abdominal Pain in Sickle Cell Anemia, Arch. Surg. **31**:607-621 (Oct.) 1935.

2. Levy, J.: Sicklemia, Ann. Int. Med. **3**:47-54 (July) 1929.

3. Murphy, R. C., Jr., and Shapiro, S.: The Pathology of Sickle Cell Disease, Ann. Int. Med. **23**:376-397 (Sept.) 1945.

4. Wintrobe, M. M.: Clinical Hematology, Philadelphia, Lea & Febiger, 1946, p. 501.

5. Huck, J. G.: Sickle Cell Anemia, Bull. Johns Hopkins Hosp. **34**: 1923, cited by Steinberg.[6]

6. Steinberg, B.: Sickle Cell Anemia, Arch. Path. **9**:876-897 (April) 1930.

7. Canby, C. B.; Carpenter, G., and Ellmore, L. F.: Drepanocytosis (Sicklemia) and an Apparently Acute Surgical Condition of the Abdomen: Report of Their Occurrence in a White Youth, with Laparotomy, Arch. Surg. **48**:123-125 (Feb.) 1944.

pains may be gradual, vague and generalized in onset or acute, excruciating and prostrating. They are usually unaccompanied with changes in abdominal muscle tone, but this is not necessarily the case. Prostrating epigastric pain associated with nausea and vomiting, rigidity, generalized tenderness and rebound may herald the onset of a crisis and be so difficult to differentiate from an acute abdominal condition requiring surgical treatment as to make operation advisable and even mandatory, with occasional catastrophic consequences.[8] Operation has been performed in 2 cases which we shall later present in detail.

THE CAUSES OF ABDOMINAL DISTRESS IN SICKLE CELL CRISIS

The cause of abdominal distress in sicklemia is an important and interesting controversial problem. Yater and Mollari[9] in 1931 suggested arterial thrombosis as one of the causes. In 1932 Leivy and Schnabel[10] pointed out that the pains resemble those of root origin, that they are neurogenic and find their cause in vertebral changes as a result of marrow hyperplasia, with compression of the bodies and pressure on the nerve roots. Campbell[1] in 1935 reported 6 cases, in 3 of which exploration gave negative results. All of the patients recovered. He pointed out that many of these patients have abdominal pain at some time and that this pain may simulate any kind of intra-abdominal visceral disorder. He believed one of the causes to be splenitis and perisplenitis, but this is not borne out by the cases of Leivy and Schnabel[10] or of Landon and Patterson.[11] Sydenstricker, Mulhern and Houseal[12] believed splenic hemorrhage to be a cause of the pain, while Cooley[13] ascribed abdominal crisis to splenic thrombosis.

Tomlinson[8a] reported on 11 patients, all of whom died and were examined at autopsy. Six of a total of 13 patients examined at autopsy

8. (*a*) Tomlinson, W. J.: Abdominal Crises in Uncomplicated Sickle Cell Anemia: A Clinico-Pathologic Study of Eleven Cases with a Suggested Explanation of Their Cause, Am. J. Med. Sc. **209**:722-741 (June) 1945. (*b*) Bauer, J.: Sickle Cell Disease, Pathogenic, Clinical and Therapeutic Considerations, Arch. Surg. **41**:1344-1362 (Dec.) 1940. Footnotes 1, 2 and 4.

9. Yater, W. M., and Mollari, M.: The Pathology of Sickle Cell Anemia: Report of a Case with Death During an Abdominal Crisis, J. A. M. A. **96**:1671-1675 (May) 1931.

10. Leivy, F. E., and Schnabel, T. G.: Abdominal Crises in Sickle Cell Anemia, Am. J. Med. Sc. **183**:381-391 (May) 1932.

11. Landon, J. F., and Patterson, H. A.: An Evaluation of Splenectomy in the Treatment of Sickle Cell Anemia: Late Results of Two Cases So Treated with a Summary of the Present Condition of All Splenectomized Patients, J. Pediat. **7**:472-477 (Oct.) 1935.

12. Sydenstricker, V. P.; Mulhern, W. A., and Houseal, R. W.: Sickle Cell Anemia: Report of Two Cases in Children, with Necropsy in One Case, Am. J. Dis. Child. **26**:132-154 (Aug.) 1923.

13. Cooley, T. B.: Indications for Splenectomy in Childhood, Journal-Lancet **54**:673-676 (Nov. 1) 1934; cited by Landon and Patterson.[11]

showed chronic hepatitis, 6 of 9 patients with abdominal crisis who died had palpable lymph nodes, 9 of 11 had fatty changes in the liver, all displayed enlargement and softening of the intestinal lymph nodes with fibrosis of the spleen and 6 had perisplenitis. The lymph nodes showed "marked hyperplasia of the reticuloendothelial cells with extensive phagocytosis of sickled erythrocytes." There was likewise marked edema of the stroma and of the endothelial cells lining the sinuses. Tomlinson summed up the clinical picture as follows:

> . . . the sudden onset of distress or pain in the abdomen usually accompanied by nausea and vomiting; rigidity or tenderness in the abdomen with occasionally pain or tenderness in the muscles or bones of the extremities not involving the joints; malaise, severe chill followed by fever, most frequently jaundice, early rather rapid peripheral vascular collapse with tachycardia, weak pulse, hyperpnea and signs of central nervous system involvement.

Patients with these symptoms, he believed, die in shock, which is secondary to sickling from anoxia, packing of capillaries by deformed red blood cells, loss of plasma and hemoconcentration.

Murphy and Shapiro [8] stated the opinion that the pains were due to vascular occlusion following thrombosis. Hemoyltic crisis is initiated by an accumulation of circulating sickle cells, with an increased tendency toward sickling as the patients grow older. These cells then precipitate out in a "simultaneous capillary blockade" and cause a crisis. They expressed the opinion that the one factor initiating the mechanism is an altered state of coagulability resulting from the increased quantities of thrombin and thromboplastin liberated after multiple repeated small infarctions.

Josephs,[14] in searching for the cause of the hemolytic anemia, decided that the red cells absorb an unknown substance common to plasma, which alters the surface tension but can be washed off with isotonic sodium chloride solution. Normal red cells will not do this. Robinson [15] ascribed the cause of the hemolytic anemia to a hyperplasia or overactivity of the cells of the reticuloendothelial system.

Bauer [8b] wrote that the hemolysis was caused by "mechanical impaction of masses of deformed red blood cells in the smaller blood vessels in various organs." He says: "This impaction with the subsequent hemolysis of the resulting conglutinated masses is responsible for the further pathologic changes and for the clinical symptoms of sickle cell anemia." He believed sicklemia to be due to an inborn, constitutional, transmitted abnormality of erythropoiesis and that the sickle cell trait

14. Josephs, H. W.: Clinical Aspects of Sickle Cell Anemia, Bull. Johns Hopkins Hosp. **43**:397-399 (Dec.) 1928; **40**:77-84 (Feb.) 1927, cited by Yater and Mollari.[9]

15. Robinson, H. A.: Sickle Cell Anemia: Etiology, with Report of a Case, J. Michigan M. Soc. **34**:388-393 (June) 1935.

represents one of the congenital stigmas associated with other congenital abnormalities. Thrombosis, ischemia, necrosis and fibrosis follow the destruction of red blood cells. Anoxemia, infection, surgical procedures and other factors slowing the circulation can initiate the whole vicious cycle of events. He reports on 1 patient with sicklemia who, after a compatible transfusion, had a reaction and died. Autopsy showed an enlarged liver and a tremendous mediastinal, tracheobronchial and abdominal lymphadenopathy caused by increase in reticular tissue. Sydenstricker, Mulhern and Houseal [12] reported hyperplasia of the mesenteric lymph nodes among other findings at necropsy in a patient who before death had complained of pain high in the abdomen.

Since 1938 we have treated 23 patients with sickle cell disease at this hospital. It is of interest to us that 8, or 34 per cent, complained chiefly of symptoms that were predominantly and recurrently gastrointestinal in nature. In this group 13 were females and 10 males, the age ranging from 1 month to 50 years [16] and averaging 12 years. The longest duration of symptoms was seventeen years. In many of these patients a crisis would begin with vague generalized abdominal pains or discomfort, the prodromal symptoms becoming typical of a relapse. In a considerable number of cases symptoms referable to the cardiovascular system were noted and frequently rheumatic fever suspected. This is easily understood in view of the associated arthralgia, prostration, fever, pain in the chest, hemic murmurs and borderline electrocardiographic findings, with roentgenologic evidence of enlargement of the heart to the right and left.

Three of the patients died. J. C. is reported on in some detail later. R. W., a woman aged 50, died of intestinal obstruction secondary to a Meckel diverticulum, and autopsy revealed splenomegaly and fibrosis of the liver and spleen, with cirrhosis of the liver. At postmortem examination M. C. showed dilatation and hypertrophy of the right side of the heart and the left auricle, dilatation of the pulmonary conus, hepatomegaly with central necrosis and engorgement of the sinusoids and periportal fibrosis with marked disease of the mesenteric lymph glands, which microscopically showed disorganization and increase in macrophages. The spleen was contracted, fibrotic, hyalinized and calcified. The cause of death was failure of the right side of the heart.

In 2 instances abdominal exploration was performed. One of the patients recovered after a stormy course in the hospital, and only after operation was it determined that he was suffering from a crisis in sickle cell anemia. Two sisters and a brother were found to be similarly affected, with a record of previous admissions to this hospital

16. Cohen, S. M.; Miller, B. W., and Orris, H. W.: Fatal Sickle Cell Anemia in a One Month Old Infant, J. Pediat. **30**:468-472 (April) 1947.

for relapses. In the other patient, a 1 month old infant known to have the disease, death occurred soon after operation. This patient was moribund when operated on. In a third case a diagnosis of acute appendicitis had been made. Operation was averted when the mother informed us that the child had sickle cell anemia and took her home. She had previously been treated in other institutions for similar complaints.

PRESENTATION OF CASES

CASE 1.—J. C.,[16] a 1 month old Puerto Rican female infant, was admitted to the hospital on July 9, 1946, with the chief complaint of fever, anorexia and irritability of one day's duration. The temperature was 104 F., the white blood cell count was 13,200, with 36 per cent polymorphonuclear cells and 64 per cent lymphocytes, and the hemoglobin content was 11.5 Gm. Urinalysis showed 3 red cells and 3 white cells per high power field. On July 9 it was noted that the child was icteric. The icterus index at that time was 130, with an immediate direct van den Bergh reaction, a serum protein content of 6.3 Gm. per hundred cubic centimeters and a cephalin flocculation reaction of 1 plus. Hematologic analysis showed a leukocyte count of 26,500, with a hematocrit value of 23 and two nucleated red blood cells per hundred white cells. There was normochromic anemia, and red cells showed anisocytosis and poikilocytosis, with occasional target cells; no spherocytosis was noted. Bleeding and clotting times were normal; the blood type was O, Rh positive. The child was given a transfusion of 50 cc. of whole blood and, because of the otitis media, placed on penicillin therapy. Two days later, wet preparation of the blood showed sickling of the red cells. There were no cold agglutinins present, and puncture of the tibial bone marrow gave negative results. On the seventh day, despite apparent improvement, the red blood cell count was 1,240,000 and the hemoglobin content 5.5 Gm., and for the following week neither showed much change.

One week later the icterus had increased. The child began vomiting and had diarrhea, was observed to moan constantly and appeared sicker. Sickling was again reported from examination of the wet preparation. At this time a mass was felt in the right upper quadrant, extending from below the liver to the umbilicus, and some abdominal distention was noted. That evening the child was markedly dyspneic. The skin was ecchymotic and mottled over the mass and the abdomen markedly distended, and a diagnosis of instussusception was made. After supportive treatment, and at the insistence of the pediatricians, laparotomy was performed and disclosed only moderately severe mesenteric adenitis. The child died four hours after operation.

Postmortem examination revealed hemorrhagic cystitis, metritis, pyelitis, renal hypertrophy with infarction and hemorrhage, hemorrhagic esophagitis and gastritis, bilateral bronchopneumonia, splenomegaly and lymphoid hyperplasia of the nodes and intestinal follicles. The small intestine was distended and contained numerous small areas of subserosal hemorrhage; there were multiple areas of superficial and deep hemorrhagic infarctions of the brain and a congenital stricture of the right ureteropelvic junction. There was an epidural hemorrhage as a result of transfusion into the sagittal sinus.

CASE 2.—S. C., a 20 year old Negro, was admitted on April 13, 1947, with a complaint of excruciating, generalized abdominal pain of four hours' duration, most marked in the lower quadrants. Bowel movements on the preceding day had

been normal, without blood, and though he had had previous attacks of abdominal pain due to what he termed indigestion, none had been as severe as this one. The past history was not suggestive of peptic ulcer.

Examination disclosed a thin, well nourished Negro writhing in pain. Physical abnormalities were confined to the abdomen, where there was boardlike rigidity and direct and rebound tenderness throughout. Roentgenologic examination of the abdomen showed an air bubble under the left hemidiaphragm, interpreted as free air. The white blood cell count was 14,700, with 89 per cent polymorphonuclear cells and 11 per cent lymphocytes. Urinalysis revealed nothing remarkable.

Shortly after his admission the patient was operated on for a ruptured peptic ulcer through a right subcostal muscle-splitting incision. The peritoneum was found free of pathologic changes except for markedly enlarged mesenteric, retroperitoneal and common duct lymph nodes. The liver was enlarged 3 to 4 fingerbreadths below the costal margin and was pale and dull, with evidence of chronic hepatitis. The stomach and duodenum were thoroughly explored, the lesser omental sac entered and the pancreas examined, and all were found to be normal. The gallbladder and the biliary tract were then manually and visually examined, and they too were found free of pathologic changes. The foramen of Winslow was almost occluded by enlarged lymph nodes in the hepatic pedicle. The wound was closed, and the patient returned to the ward in critical condition. He was treated with gastric suction, intravenous administration of fluids, oxygen, sodium sulfadiazine and large doses of penicillin. On the following day, an examination of the blood by the laboratory showed notable sickling of the red blood cells at the end of thirty minutes and twenty-four hours, with a total red blood cell count of 1,500,000, a hemoglobin content of 8.5 Gm. and 11 normoblasts per hundred white blood cells. The red cells showed anisocytosis and poikilocytosis, and a diagnosis of crisis in sickle cell anemia was made.

The past history revealed that the patient had been hospitalized for hepatitis while in the navy. A summary of his course in the naval hospital revealed that on April 13, 1946, he was admitted with a diagnosis of infectious hepatitis, confirmed by laboratory findings of hepatic insufficiency. Blood studies at that time were not remarkable, and no wet preparations had been examined. Liver function tests were regularly repeated until October 1946, when the reactions were found to be normal and he was discharged for duty.

Hematologic survey of other members of his family at this time revealed that 2 sisters and 1 brother had the sickling abnormality.

His further course in our hospital was uneventful until the fifth postoperative day, when he had a severe reaction to a transfusion of 250 cc. of matched whole blood. He responded rapidly to supportive treatment, and on the nineteenth day after his admission he was discharged to the outpatient department for follow-up care.

CASE 3.—V. R., an 8 year old Negro girl, was admitted to the hospital on Oct. 7, 1943, with a complaint of sudden onset of periumbilical pain which was sharp, recurrent and unrelieved by nausea and vomiting. Examination showed an acutely ill patient. There was slight abdominal distention, with spasticity throughout, and deep tenderness, but no rebound, was present in the right lower quadrant and periumbilically. There was no palpable mass or viscus. The white blood cell count was 25,000, with 81 per cent polymorphonuclear cells, 3 per cent stab cells, 1 per cent eosinophils and 15 per cent lymphocytes. The chest and the urine were normal, and a diagnosis of acute appendicitis was made.

While awaiting the consent of the mother to operation, we were notified that the child had been known to have sickle cell anemia for the past five years and had suffered previous similar attacks. Operation was postponed, and the child was later taken home by her mother.

COMMENT

We should like to postulate as one of the causes of abdominal pain in sickle cell crisis a mesenteric and retroperitoneal lymphadenitis and lymphadenopathy, noted in each of the 2 patients examined and at autopsy in 2 others and previously noted.[17] Whether this is the result of intercurrent infection of the upper respiratory tract, as may well have been the case in regard to our first patient (J. C.), or whether it is part of the picture of reticular hyperplasia so frequently noted in the abdominal lymph nodes of these persons in crisis is difficult to say. Hematopoiesis has also been suggested as a cause. It is understandable that this frequently noted lymphadenopathy may give rise to pain, as does the mesenteric adenitis following an infection of the upper respiratory tract, when the nodes are inflamed and swollen. We believe further that thrombotic episodes, coexistent hepatitis and hepatosis, splenitis and perisplenitis may be secondary causes. The frequency of hepatic dysfunction associated with the disease has been previously noted.[18] Many cases are characterized by positive cephalin flocculation reactions, and pathologic changes in the liver are repeatedly noted at operation and autopsy. Lowe and Adams [18a] ascribed the hepatomegaly to stagnation of sickle cells in the hepatic sinusoids, with increased phagocytic activity of the Kupffer cells, parenchymal edema and degeneration. Stasney [18b] found the liver to be enlarged, red, brown and firm. There was congestion, distention of the sinusoids and swelling of the Kupffer cells associated with erythrophagocytosis and hemosiderosis. Ryerson and Terplan [18c] described a case in which a diagnosis of subacute liver atrophy was confirmed when autopsy was performed, and Dale [18d] mentioned 2 more.

We were interested in utilizing the recently developed Winsor-Burch parameter test [19] for the diagnosis of sickle cell anemia, and in

17. Syndenstricker and others.[12] Robinson.[15] Bauer.[8b]

18. (*a*) Lowe, R. C., and Adams, C. C.: Studies on the Pathophysiology of Sickle Cell Disease, Ann. Int. Med. **22**:192-200 (Feb.) 1945. (*b*) Stasney, J.: Erythrophagocytosis and Hemosiderosis in the Liver and Spleen in Sickle Cell Disease, Am. J. Path. **19**:225-237 (March) 1943. (*c*) Ryerson, C. S., and Terplan, K. C.: Sickle Cell Anemia: Two Unusual Cases with Autopsy, Folia hæmat. **53**:353-369, 1935; cited by Bauer.[8b] (*d*) Dale, G. C.: Sickle Cell Anemia, South. Med. & Surg. **99**:14-16 (Jan.) 1937, cited by Bauer.[8b] Levy.[2]

19. (*a*) Winsor, T., and Burch, G. E.: Sickle Cell Anemia, "A Great Masquerader," Easily Recognizable with Routine Use of Diagnostic Parameter, J. A. M. A. **129**:793-796 (Nov.) 1945; (*b*) Diagnostic Psysiochemical Blood Tests in Sickle Cell Anemia, Am. J. M. Sc. **207**:152-160 (Feb.) 1944.

our last patient the reaction was decidedly positive on two occasions, to the extent where differences in sedimentation rates between anoxic and well oxygenated blood was 47 mm. per hour in the first determination and 92 mm. per hour in the second. We used the aeration-tourniquet technic.

SUMMARY

The crisis in sickle cell disease must be considered in the differential diagnosis of an acute abdominal condition requiring surgical treatment if unnecessary laparotomy is to be avoided.

The abdominal distress seen in sickle cell crisis is undoubtedly due to one or more of several factors, including mesenteric lymphadenopathy, splenic and hepatic thrombosis, vascular occlusions in the tissues of the abdominal wall, hepatitis and hepatosis and possibly neurogenic factors resulting from rarefaction of vertebral bodies with pressure on the roots.

We concur with Bauer [8b] and with Winsor and Burch [19a] in the belief that all Negroes deserve a routine examination of the wet preparation of the blood on their admission to the hospital to rule out sicklemia when there is any question of the diagnosis of an abdominal condition requiring surgical treatment. This is hardly of less importance than a routine blood count. Certainly when the familial and past histories suggest the presence of the disease or when icterus, hepatomegaly or abdominal pain is noted, the hanging drop preparation should be examined for sickling.

We have presented 3 patients in whom the manifestations of sickle cell crisis were largely abdominal and in 2 of whom laparotomy was performed.

ECHINOCOCCAL CYSTS OBSTRUCTING THE COMMON BILE DUCT

Report of Case

THOMAS N. POORE, M.D.
CHARLES P. MARVIN, M.D.
AND
WALTMAN WALTERS, M.D.
ROCHESTER, MINN.

ECHINOCOCCAL or hydatid cysts, especially in the liver, may attain great size without the production of prominent symptoms. It has been estimated that about 25 per cent of human beings infested with echinococci go through life without any symptoms or complaints referable to them.[1] In most cases, however, symptoms do appear, and often these are bizarre. It is the purpose of this paper to review some of the literature on echinococcal cysts which have caused obstruction of the common bile duct, to report data on 40 cases in which the diagnosis of primary echinococcal cysts of the liver was made and proved at the Mayo Clinic and to report an illustrative case in which a hydatid cyst ruptured into the biliary tract and gave rise to symptoms indicative of stone in the common duct.

About 70 per cent of primary echinococcal cysts are found in the liver and four of every five echinococcal cysts of the liver are in the right lobe.[2] Such a cyst may continue to grow for many years or for the life of the person affected without producing any signs except enlargement of the liver and the accompanying subjective symptoms, such as a sensation of weight or dragging in the upper part of the abdomen. More rarely symptoms of pressure, such as nausea, vomiting, jaundice, respiratory distress and even cardiac embarrassment may occur. A cyst of the liver may suppurate and then produce the clinical picture of hepatic abscess. The cyst may rupture into a large bile duct, with

From the Division of Surgery, Mayo Clinic.

1. Napier, L. E.: Hydatid Disease, in the Principles and Practice of Tropical Medicine, New York, The Macmillan Company, 1946, pp. 737-746.

2. Barnett, L.: Hydatid Cysts: Their Location in the Various Organs and Tissues of the Body, Australian & New Zealand J. Surg. **12**:240-248 (April) 1943.

the production of biliary colic, into the peritoneal cavity, into the lung, pleura or bronchus or into a kidney, with the production of renal colic.

The association of jaundice with echinococcal cysts of the liver was first noted by Neisser [3] in 1877. Since then many studies of this condition have been made. However, few reports have appeared in North American literature. It should be noted that jaundice is rarely caused by direct compression of the bile ducts by an enlarging cyst. More often jaundice is due to embolic obstruction of the ducts by mother or daughter cysts, by portions of the cyst wall or by other debris coming from the mother cyst. Jaundice is then accompanied with colicky pain in the right upper part of the abdomen, and this syndrome has been referred to as "pseudolithiasis." [4]

Even more dangerous to the patient than the biliary obstruction is the suppuration in the mother cyst which is likely to ensue after intrabiliary rupture. This is the most common cause of suppuration within the primary cyst, and in some series rupture has been found in all cases in which suppuration occurred. The evacuation of the cyst and its walls into the biliary tract is not usually complete, but at times it may be, and spontaneous cure may result. Mason and Barnett [5] reported the passage of a complete thin-walled mother cyst through the bile ducts of a child. Jaundice and such severe colic were associated that exploratory operation was carried out. The patient subsequently vomited a ruptured cyst the size of a small tangerine. Duprey [6] claimed that 24 per cent of the patients are cured by drainage of the cyst through the bile ducts. An even higher percentage of cures were reported in cases in which the echinococcal cysts of the lung had spontaneously ruptured into a bronchus.

"Pseudolithiasis" is not an easy condition to diagnose. It is frequently missed even at exploratory operation. A dilated common duct is found, but there is no other evidence of gallstones. Subsequently, portions of the cyst may appear in drainage from the bile ducts. Even in regions in which the disease is relatively common a correct preoperative diagnosis is made in less than 50 per cent of the cases.[1]

3. Neisser, cited by Gennaro, J. F.: Echinococcus Cyst of the Liver Simulating a Stone in the Common Bile Duct, J. Internat. Coll. Surgeons. **3**:342-350 (Aug.) 1940.

4. Reyes, M., and Derqui, M.: Quiste calcificado de hígado a forma pseudolitiásica, Bol. y trab., Soc. de cir. de Buenos Aires **21**:768-774 (Sept. 15) 1937.

5. Mason, A. J., and Barnett, L.: Spontaneous Evacuation of a Hydatid Cyst of the Liver by Way of the Bile Ducts, Australian & New Zealand J. Surg. **7**:78-80 (July) 1937.

6. Duprey, G., cited by Dévé.[10]

There are several points of special note in establishing the diagnosis. About 95 per cent of the persons who have hydatid cysts in North America are immigrants, especially those from Italy, Iceland, Greece and Germany.[7] However, the incidence of the disease in its classic home, Iceland, has been greatly reduced.[8] The patients who have intrabiliary rupture of their cysts are usually younger than those who have cholelithiasis. The incidence of intrabiliary rupture of echinococcal cysts among males and females is about equal. The skin tests and the complement fixation test for echinococcosis are relatively simple to perform and are reliable. The greatest difficulty involved is the acquisition of fluid from a hydatid cyst for use as the antigen. The eosinophilia, which was great in the case which we are reporting, is suggestive of the diagnosis, but this is found in less than 25 per cent of patients with echinococcosis. With intrabiliary rupture of a cyst, hydatid material may be found in the stools, in vomitus or in material obtained by duodenal aspiration. Such a finding is of great value in establishing the diagnosis.

Dew [9] stated that some degree of intrabiliary rupture is the commonest complication of echinococcal cysts of the liver. Dévé,[10] however, regarded intraperitoneal rupture as the most frequent complication and gave the figure for intrabiliary rupture as only from 5 to 10 per cent of all hepatic hydatid cysts. The incidence of rupture into the bile ducts appears to be much greater in the cases in which the diagnosis has been made at the Mayo Clinic.

The case records of all patients seen at the clinic whose condition was diagnosed as echinococcosis were studied. The liver of 40 of these patients was proved to be the site of the primary cyst. Such proof was based on a combination of history, positive reaction to the skin test, clinical findings and anteroposterior and lateral roentgenographic views of the region of the liver or on the finding of a hydatid cyst at the time of operation. Application of these criteria caused us to exclude many probable cases of hydatid cysts of the liver. Of the 40 patients, 14 (35 per cent) gave a definite history of severe biliary

7. Magath, T. B.: Hydatid Disease (Echinococcus) in North America, Pennsylvania M. J. **44**:813-819 (April) 1941.

8. Ofeigsson, O. J.: Hydatid Disease in Iceland, Proc. Staff Meet., Mayo Clin. **12**:420-421 (July 7) 1937.

9. Dew, H. R.: Hepatic Cysts Involving the Biliary Passages, in Hydatid Disease; Its Pathology, Diagnosis and Treatment, Sydney, The Australian Medical Publishing Company, Ltd., 1928, pp. 168-181.

10. Dévé, F.: Echinococcose hépatique (kystes hydatiques du foie), in Roger, G. H.; Widal, F., and Teissier, P. J.: Nouveau traité de médicine, Paris, Masson & Cie, 1928, vol. 16, pp. 775-805.

colic at some time during the course of their disease. Thirteen of the 14 also gave a history of jaundice during some of their attacks of biliary pain.

All 14 patients were operated on. The patient who did not have jaundice was found to have gallstones and a moderate-sized hydatid cyst of the liver. It is interesting to speculate on the origin of the gallstones in this case, as to whether or not they may have arisen from a nidus of debris from a hydatid cyst.

Another 10 of the 40 patients (25 per cent) gave a history of mild or indefinite pain in the right upper abdominal quadrant during the period of their illness. Dew [9] stated that he was convinced that practically all the so-called painful types of apparently uncomplicated hydatid cysts of the liver are in reality due to minor ruptures, with passage of small pieces of debris or membrane into the ducts. He considered that this is a more likely explanation for the pain than hepatoptosis, pressure on the ducts, visceral distention or pressure on the celiac plexus.

The remaining 16 patients (40 per cent), although they had primary echinococcal cysts of the liver, either had no complaints referable to the biliary tract or had such vague complaints as bloating, indigestion or nausea and vomiting.

REPORT OF A CASE

The patient, an itinerant Greek immigrant 54 years old, had been seen at the clinic on ten previous occasions. He had been treated for latent syphilis, recurring gonorrheal urethritis, traumatic paralysis of the right opponens pollicis muscle, chemical burn of the conjunctiva, presbyopia and ecthymatous ulcers. In 1936, when he was seen at the clinic for the first time, a cholecystogram was made because of the complaint of pain in the right upper quadrant of the abdomen. It was found that the gallbladder functioned normally, but multiple areas of calcification were noted which, in lateral views, were shown to be in the liver. Reactions to the Casoni intradermal test and the complement fixation test with fluid from a hydatid cyst as antigen were both strongly positive. Blood smears disclosed an eosinophil content of 15.5 per cent. A diagnosis of calcified echinococcal cysts of the liver was made.[11] Because of the positive results of serologic tests for syphilis (Kline test grade 4 and Kahn test grade 4 on a grading basis of 1 to 4, reaction to Hinton test negative and Wassermann reaction strongly positive), operation was postponed for one month while antisyphilitic treatment was started. At the end of the month the patient had improved greatly and refused operation.

In June 1947, eleven years later, the patient returned to the clinic and was hospitalized for emergency treatment. The following history was obtained: Thirteen days previously severe, cramping, intermittent pain had begun gradually in the right upper quadrant of the abdomen and had continued for three days.

11. Smith, H. L., and Magath, T. B.: Calcified Echinococcus Cysts in the Liver: Report of Case, Proc. Staff Meet., Mayo Clin. **12**:405-408 (June 30) 1937.

This pain was superimposed on a dull, severe, constant pain of the right upper abdominal quadrant which had commenced at the time of the crampy pain and continued until the present admission. Morphine given by his physician had produced only temporary relief. The pain extended through the back, to the right axilla and across the chest to the left axilla. Vomiting had occurred at the onset but had ceased after two days. Jaundice had not been noted by the patient, but he had noticed that since the second day of the attack his urine had been dark and his stools light in color. There was no pruritus. Anorexia and chilly sensations had been present early in the illness but had subsided. For two years he had had episodes of dull precordial tightness which lasted about one hour. This was unrelated to exertion. He reported three previous episodes similar to his presenting complaints, one in 1936, one in 1937 which lasted about one hour, and one in 1946 which lasted three or four hours. Although the pain was similar in these episodes, he recalled no signs of jaundice.

On admission the patient appeared acutely ill and was moaning at intervals. Icterus was pronounced. The systolic blood pressure was 100 mm. of mercury and the diastolic 62 mm. The pulse rate was 84 and the temperature 99.8 F. There was some guarding in the right upper quadrant of the abdomen and pronounced but poorly localized tenderness in the region of the gallbladder. The liver was palpable down to 6 cm. below the right costal margin. No hydatid thrill was noted. The remainder of the history and physical examination was noncontributory.

The laboratory findings were reported as follows: The urine had a specific gravity of 1.010 and contained a moderate amount of albumin and a small amount of pus. There was 16 Gm. of hemoglobin per hundred cubic centimeters of blood. The erythrocytes numbered 5,500,000 and the leukocytes 9,800 per cubic millimeter of blood. There was an eosinophil content of 34 per cent. The Kline, Kahn, Hinton and Kolmer tests all gave negative results. The value for serum bilirubin was 6.6 mg. direct and 2.4 mg. indirect per hundred cubic centimeters. The prothrombin time (Quick) was 21 seconds, and the cephalin-cholesterol test gave negative results. The value for total cholesterol was 254 mg. and cholesterol esters 102 mg. per hundred cubic centimeters of plasma. The blood urea was 32 mg. per hundred cubic centimeters, and the sedimentation rate (Westergren) was 24 mm. per hour. The plasma protein content was 7 Gm. per hundred cubic centimeters. The stools were acholic. An electrocardiogram showed a slurred QRS complex in lead III and positive T waves in leads CR_3 and CR_4. Roentgenograms of the thorax showed nothing remarkable, and one of the upper part of the abdomen revealed evidence of a large cystic lesion with calcification of its walls in the right lobe of the liver. The colloidal gold curve of the spinal fluid was 0111100000.

Four days after the patient's admission to the hospital the stools were still acholic, but on the fifth day duodenal drainage yielded dark green bile, the stools became greenish colored and the value for serum bilirubin fell slightly to 6.3 mg. direct and 0.9 mg. indirect.

Twelve days after the patient was admitted, on July 3, 1947, operation was performed by one of us (W. W.) through an upper right rectus incision. A large echinococcal cyst approximately 10 cm. in diameter occupied the right lobe of the liver. Half of this cyst projected from the lower portion of the right lobe and was calcified in places. The cyst was opened. The daughter cysts were removed, and the cyst was unroofed. A double strip of plain gauze was placed in the cyst cavity, as was a rubber tube for the introduction of solution of

formaldehyde. No stones could be felt in the gallbladder, but the wall was thickened and somewhat edematous. No stones could be felt in the common bile duct, which was dilated to about twice normal size. The gallbladder was opened, and no stones were found; a dressed tube was then placed in the gallbladder. The common bile duct was opened and black tarry bile with cholesterin crystals drained out. Three echinococcal cysts, each about 1.5 cm. in diameter, were removed from the common bile duct. Scoops were then passed through the lower end of the duct into the duodenum without encountering obstruction. Exploration of the intrahepatic ducts disclosed nothing. The head of the pancreas was enlarged to about twice normal size; this enlargement appeared to be due to pancreatitis. A T tube was placed in the common bile duct, and four Penrose drains were placed in the abdomen, which was then closed. The pathologist verified the surgical findings; many of the daughter cysts showed numerous scolices with horny hooklets.

The postoperative course was rather stormy. At no time was the patient in any danger, but he suffered from numerous pains and a temperature up to 103 F. on the third, fourth and fifth postoperative days. The cystic cavity in the liver was irrigated on the second, third and fourth days with a 2 per cent solution of formaldehyde. The patient's temperature was normal for the first time on the fourteenth day. The T tube was clamped for longer periods each day. A cholangiogram taken on the seventeenth day showed that the common duct was normal in size. The contrast medium entered the duodenum freely. The T tube was then removed.

The hepatic cyst was irrigated on alternate days with solutions of penicillin and streptomycin. Three months after operation there had been no appreciable change in the size of the cyst. The general condition of the patient, however, was excellent. He had gained weight, was free of jaundice, had no pain and had a good appetite. He was then dismissed from observation at the clinic. At the time of writing, seven months after operation, efforts to contact him were unsuccessful.

SUMMARY

In the case reported daughter echinococcal cysts had caused obstruction of the common duct. The clinical records of 40 patients who had proved primary hydatid cysts of the liver were studied. Fourteen of these patients (35 per cent) gave a definite history of severe biliary colic. Thirteen of the 14 had been jaundiced. Ten (25 per cent) gave a history of mild or indefinite pain in the right upper quadrant during the period of their illness. Sixteen (40 per cent) had no complaints referable to the biliary tract, although they had primary hepatic cysts.

CHRONIC CHOLECYSTITIS PRODUCED BY DIVISION OF THE SPHINCTER OF ODDI

S. H. GRAY, M.D.
J. G. PROBSTEIN, M.D.
AND
LEO A. SACHAR, M.D.
ST. LOUIS

IN AN EARLIER communication [1] it was shown that division of the sphincter of Oddi of dogs was followed by the appearance of diastase in the bile obtained from cholecystostomy tubes placed in such dogs. Normally, bile contains no diastase or negligible amounts of it. The effects of a prolonged reflux of duodenal contents into the gallbladder were obscured by the irritative effect of the cholecystostomy tube.

The present experiments were designed to determine (1) whether section of the sphincter of Oddi is followed by reflux of duodenal contents into the gallbladder when the latter is not decompressed by a cannula and (2) what the effects are of prolonged duodenal reflex through an incompetent sphincter of Oddi.

Observations relating to these problems have been described by Colp, Doubilet and Gerber.[2] These authors divided the sphincteric mechanism of the common duct of 3 dogs by inserting a specially designed sphincterotome through an opening in the gallbladder and thence through the common duct. The opening into the gallbladder was closed with a purse string suture. After eight, thirty and one hundred and fifty days the dogs were killed. The gallbladder of the dog sacrificed after eight days showed an acute inflammation. In the other 2 dogs there were acute and chronic inflammatory changes in the wall of the gallbladder. Further observations have been made by Mallet-

Aided by the David May-Florence G. May Fund.

From the Laboratory and Department of Surgery of the Jewish Hospital of St. Louis, and the Department of Surgery, Washington University School of Medicine.

1. Gray, S. H.; Heifetz, C. J.; Probstein, J. G., and Russi, S.: Effect of Division of Sphincter of Oddi on Bile Diastase of Dog, Arch. Surg. **47**:160 (Aug.) 1943.

2. Colp, R.; Doubilet, H., and Gerber, I. E.: Endocholedochal Section of Sphincter of Oddi, Arch. Surg. **33**:696 (Oct.) 1936.

Guy and his co-workers,[3] who transected the sphincter of Oddi of 8 dogs, employing a transduodenal approach. These dogs were observed for periods of eighty-three to three hundred and seventeen days. A marked inflammatory reaction in the wall of the common duct and chronic cholecystitis were observed when the dogs were killed. Precipitation of calculi was noted in 4 cases. In another paper Mallet-Guy and Auger[4] found that less histologic changes in the gallbladder developed in a dog which was subjected to a pyloric exclusion procedure as well as section of the sphincter of Oddi than in 2 other dogs subjected to division of the sphincter of Oddi alone.

EXPERIMENT

Ten normal, apparently healthy mongrel dogs were anesthetized with sodium pentobarbital, given intravenously. The abdomen was entered through an upper midline incision. The gallbladder was aspirated and the bile obtained was analyzed for diastase[5] provided it was not blood tinged. The opening of the common duct into the duodenum was exposed transduodenally. With one blade of a scissors inserted into the duct opening and the other on the duodenal mucosa, the duct was opened along its intramural course for a distance of about 1 cm. It should be noted that the procedure employed results in division of both components of the sphincter mechanism at the termination of the common duct, the sphincter of Oddi proper and the duodenal musculature which compresses the intramural portion of the duct. In this paper the term "sphincter of Oddi" is used to refer to the entire sphincter mechanism. Occasionally the same effect was secured by inserting a small curved hemostat into the opening of the ampulla and then cutting down on the slightly opened forceps tips with a small scalpel blade. The duodenum was then closed with one layer of fine intestinal sutures. The abdominal wall was closed in layers with nonabsorbable sutures.

At intervals ranging from four to eighty-six weeks after this initial operation the dogs were again anesthetized. The gallbladders were aspirated and the diastase concentration in the bile determined. Pieces of liver, pancreas, gallbladder and common duct were removed for microscopic study and the dog killed.

RESULTS

Only 2 of the 10 specimens of bile obtained at the time of the initial operation were considered suitable for diastase determination. These

3. Mallet-Guy, P.; Auger, L., and Billa, M.: Compt. rend Soc. de biol. **112**:899, 1933.

4. Mallet-Guy, P., and Auger, L.: Lyons Chir. **29**:629, 1932.

5. Somogyi, M.: J. Biol. Chem. **125**:399, 1938.

contained 0 and 150 units respectively. This last value is slightly higher than any previously reported by Gray, Probstein and Heifetz but is still negligible in comparison with the amount of diastase in a dog's blood.

The diastase activity of the gallbladder bile obtained at the second operation, weeks after the division of the sphincter of Oddi, is given in the accompanying table. Grossly, the gallbladders all appeared normal at the time of the initial operation.

The anatomic and histologic observations are given in detail in the following paragraphs.

Dog 20.—This dog was killed four weeks after division of the sphincter. The opening of the common duct into the duodenum was wide. The gallbladder and the extrahepatic biliary ducts appeared normal. Sections of the gallbladder showed a chronic inflammatory reaction consisting of round cells and plasma cell infiltration, with some edema.

Diastase Activity of the Gallbladder Bile

Dog	Weeks from Operation to Day Killed	Preoperative Concentration of Diastase, Units	Postoperative Concentration of Diastase, Units
20	4	...	131
18	4	...	125
15	8	150	1,420
11	12	...	0
10	16	...	...
8	20	...	4,700
4	24	0	Insufficient quantity*
6	30	...	240
21	86	...	Insufficient quantity
22	89	...	770

* The gallbladder contained matted hair, and bile could not be aspirated.

The serosa of the gallbladder was somewhat thickened. The sections of liver showed no inflammatory changes.

Dog 18.—This dog was killed four weeks after division of the sphincter. Grossly the gallbladder, liver and extrahepatic ducts appeared normal. In sections of the gallbladder there was dilatation of the subserosal lymphatic vessels. Section of the liver showed collections of large mononuclear cells, among which were a few plasma cells in the portal triads.

Dog 15.—This dog was killed eight weeks after division of the sphincter. At necropsy the gallbladder appeared thickened. The common duct was much thickened, particularly in the distal 2 cm. The entrance of the common duct into the duodenum was wide open. When the gallbladder was examined it was found to contain eight tan-colored concretions, each measuring 0.5 by 1 cm. Microscopic sections of the gallbladder showed the wall to be three or four times the normal thickness, owing primarily to edema in the muscularis and the submucosal

layers. The subserosal lymphatic vessels were dilated. There was a minimal infiltration of round cells into the muscularis and subserosa. Section of the liver showed no inflammatory reaction. The common duct epithelium was thrown into folds. There was a slight increase in connective tissue about the duct. The concretions were analyzed by Dr. M. Somogyi and reported to be almost entirely of calcium phosphate.

Dog 11.—This dog was killed twelve weeks after division of the sphincter. Grossly and microscopically the liver and the gallbladder appeared normal.

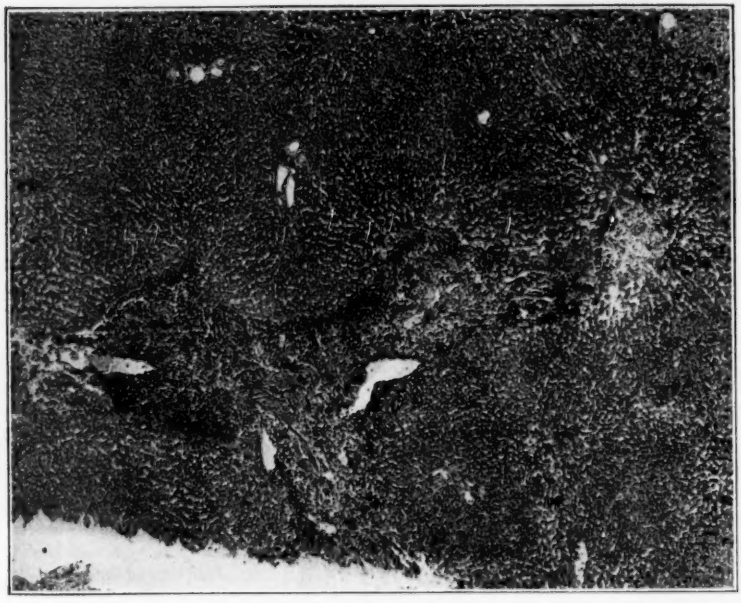


Fig. 1.—Section of liver of dog 8, killed twenty weeks after division of sphincter of Oddi, showing suppurative cholangitis.

Dog 10.—This dog was killed sixteen weeks after division of the sphincter of Oddi. At necropsy the opening of the common duct into the duodenum appeared essentially the same as it was before the sphincter was cut. The gallbladder, liver and common duct appeared normal grossly. Microscopic sections showed a normal gallbladder, liver and common duct.

Dog 8.—Dog 8 was killed twenty weeks after the division of the sphincter of Oddi. This dog was delivered of pups one month before she was killed. At necropsy the gallbladder and common duct appeared

Fig. 2.—Normal gallbladder of a dog.

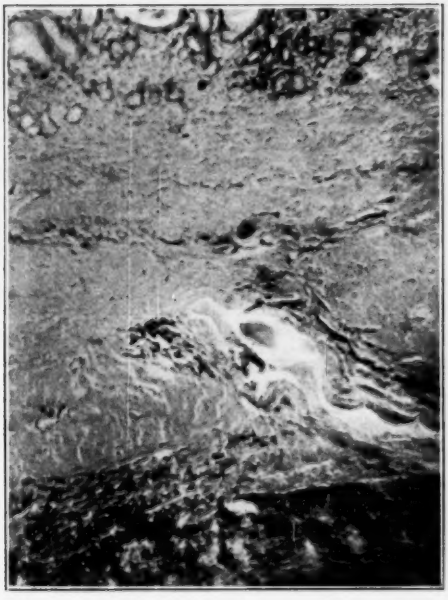


Fig. 3.—Gallbladder of dog 4 six months after division of sphincter of Oddi. (Same magnification as in figure 2).

thickened. The ampulla was wide open. Microscopic sections showed a markedly thickened gallbladder wall. All layers were increased in depth. The muscularis was hypertrophied, somewhat edematous and infiltrated with lymphocytes. The subserosa was thick and consisted of old connective tissue. There was a large number of mitotic figures in the mucosal cells. Sections of the liver showed acute hepatitis, with abscess formation. The portal spaces were infiltrated with polymorphonuclear cells (fig. 1). Sections of the common duct showed an increased amount of connective tissue about the ducts. The epithelium

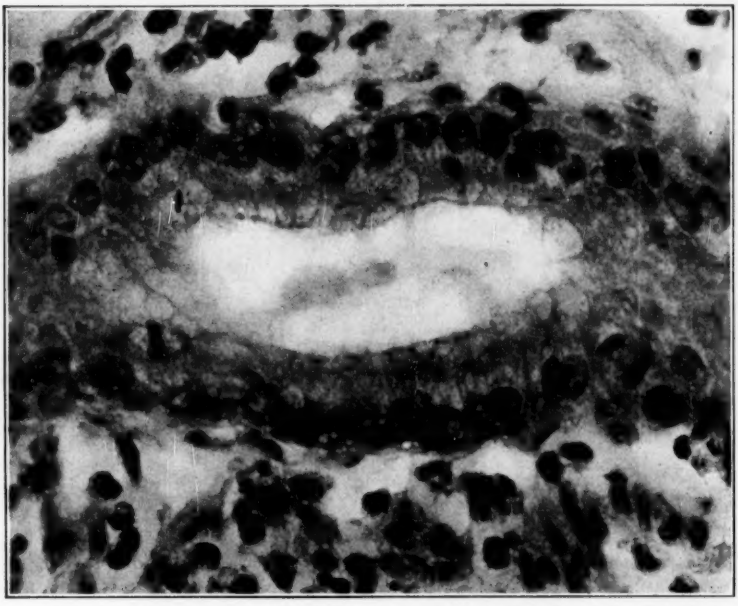


Fig. 4.—High power view of gallbladder mucosa of dog 4, showing frequent mitotic figures.

was thrown into folds. There were frequent mitotic figures in the mucosal cells. Many round cells were seen throughout the wall of the duct.

Dog 4.—Dog 4 was killed twenty-four weeks after the sphincter was divided. At necropsy the gallbladder and common duct appeared markedly thickened. The gallbladder could not be aspirated. When it was opened, it was found to contain matted hair. The entrance of the common duct into the duodenum was wide open. Microscopically the gallbladder resembled that of dog 8. The wall was markedly thick-

ened and infiltrated with round cells (fig. 3). Again the frequency of mitotic figures in the mucosal cells was striking (fig. 4). The microscopic sections of the liver showed no evidence of inflammation. The sections of the common duct revealed some increase in connective tissue, with a mild inflammatory reaction in the surrounding connective tissue.

Dog 6.—Dog 6 was killed thirty weeks after the sphincter was cut. Grossly the gallbladder appeared normal. The common duct appeared more distinct than usual. Microscopically the gallbladder and liver appeared normal. There was possibly a slight increase in connective tissue about the common duct. The epithelium was thrown up into folds.

Dog 21.—This dog was killed eighty-six weeks after the sphincter was cut. During the interim the animal had apparently been in good health. At necropsy a small shrunken gallbladder was found. The common duct was grossly thicker than normal. The opening of the common duct into the duodenum was patulous. Microscopically the liver showed a mild infiltration of polymorphonuclear cells about the small bile ducts. There was a small abscess. The gallbladder was thickened by fibrous tissues laid down mainly in the subserosa.

Dog 22.—This dog was killed eighty-nine weeks after the sphincter was cut. The opening of the common duct into the duodenum was patulous. The gallbladder was grossly and microscopically thickened. There were numerous lymphoid follicles beneath the epithelium. The liver appeared normal grossly and microscopically.

COMMENT

After transduodenal division of the sphincter of Oddi and division of a portion of the intramural wall of the common duct, a wide opening persists, permitting duodenal contents to regurgitate as high as the gallbladder. The presence of large amounts of diastase in the gallbladder bile after, but not before, the sphincter of Oddi is divided and the finding of hair in the gallbladder of 1 dog substantiate this statement. As described earlier,[6] division of the sphincteric mechanism of the common duct is followed by chronic inflammatory changes in the gallbladder and the common duct. In our experiments these changes were most marked in cases in which the duodenal reflux was the greatest, as shown by higher concentrations of diastase in the gallbladder. In 3 of the 10 dogs hepatitis ensued. This suggests that the division of the sphincter of Oddi in human beings for therapeutic purposes in cases of recurrent pancreatitis should be approached with caution.

6. Colp and others.[2] Mallet-Guy and others.[3] Mallet-Guy and Auger.[4]

High diastase levels have been found in human gallbladder bile on some occasions. In recent years the suggestion has been made that pancreatic juice or duodenal contents may cause disease by entrance into the upper part of the common duct and gallbladder.[1] It is not apparent whether the inflammatory changes observed in these experiments are due to the action of activated pancreatic enzymes or to bacterial action or to both. Mallet-Guy, Auger and Billa [3] found that after transection of the sphincter of Oddi in the dog, the gallbladder bile contains Bacillus coli and Streptococcus viridans, as well as other habitual residents of the intestine.

The significance of the large number of mitotic figures in the mucosal cells observed in 2 cases is not known. It is of interest that the pathologic changes in the gallbladder induced by regurgitation up the common bile duct consist chiefly of subserosal fibrosis and that Luschka's ducts, which so frequently characterize human chronic cholecystitis, were not found in these gallbladders.

The experimental production of chronic cholecystitis by division of the sphincter of Oddi in dogs suggests that some cases of chronic cholecystitis in human beings might possibly be due to an incompetent sphincter mechanism at the opening of the common duct into the duodenum.

SUMMARY

When the sphincter of Oddi in dogs was divided transduodenally, duodenal contents regurgitated into the gallbladder. Chronic cholecystitis and, occasionally, acute hepatitis ensued. Numerous mitotic figures were found in the mucosa of two gallbladders.

THRESHOLD OF THERMAL TRAUMA AND INFLUENCE OF ADRENAL CORTICAL AND POSTERIOR PITUITARY EXTRACTS ON THE CAPILLARY AND CHEMICAL CHANGES

An Experimental Study

OLIVER COPE, M.D.
JOHN B. GRAHAM, M.D.
GEORGE MIXTER Jr., M.D.
AND
MARGARET R. BALL, A.B.
BOSTON

WITHIN the few years prior to the entry of the United States into World War II there was a growing conviction that adrenal cortical extract was beneficial in the treatment of burn shock. From 1933, when Swingle and others [1] first called attention to the similarity of adrenal insufficiency and shock, there appeared numerous reports of the efficacy of both adrenal cortical extract and desoxycorticosterone acetate in various forms of experimental and clinical shock. Among others, Scudder and Elliott [2] reported benefit from the use of adrenal cortical extract in the care of victims of the Hindenberg dirigible disaster who suffered from shock after burns, and Rhoads, Wolff and Lee [3] expressed the belief that they had observed a plasma-sparing effect of the extract in burned patients. The point of view that adrenal cortical therapy was beneficial in shock seemed plausible, particularly when the shock was due to burns, since the salient physiologic disorder of a thermal injury had been demonstrated to be an increased capillary

This work was aided by a grant from the Ciba Pharmaceutical Products, Inc., Summit, N. J.

From the Surgical Research Laboratories of the Harvard Medical School at the Massachusetts General Hospital.

The work described in this paper was done under a contract, recommended by the Committee on Medical Research, between the Office of Scientific Research and Development and Harvard University.

1. Swingle, W. W.; Pfiffner, J. J.; Vars, H. M.; Bott, P. A., and Parkins, W. M.: The Function of the Adrenal Cortical Hormone and the Cause of Death from Adrenal Insufficiency, Science **77**:58, 1933.

2. Scudder, J., and Elliott, R. H. E., Jr.: Controlled Fluid Therapy in Burns, South. Med. & Surg. **104**:651, 1942.

3. Rhoads, J. E.; Wolff, W. A., and Lee, W. E.: The Use of Adrenal Cortical Extract in the Treatment of Traumatic Shock of Burns, Ann. Surg. **113**:955, 1941.

permeability and because there was experimental evidence suggesting an increased capillary permeability in adrenal insufficiency.[4] Lymph draining from peripheral tissues of dogs suffering from adrenal insufficiency had been demonstrated to have a high protein concentration, one possible explanation of which was an increased capillary permeability.

Neither the clinical nor the experimental observations of the efficacy of adrenal cortical extract in shock were so unequivocal that the concept could be accepted without confirmation. In several of the reports an alternative explanation could be suggested for the positive finding. In the patients the burns and the subsequent wound infections were by no means equal and comparable, and in their care measures other than administration of adrenal cortical extract had been employed. For the experimental findings which lead to the suggestion that the capillaries are more permeable in adrenal cortical insufficiency, an alternative explanation is tenable. The observed increase of the protein concentration in peripheral lymph could be explained on the basis of dehydration. However, even if the hormone of the adrenal cortex exerted no direct influence on the capillary membrane, it might influence renal or metabolic function in such a way as to relieve a load placed on the organism by trauma.

In view of the importance for the care of casualties in World War II of any measure leading to improvement in the therapy of burns, investigation into the use of adrenal cortical hormone substances in the therapy of burn shock was indicated. Two approaches to the study were possible—a physical one through capillary permeability and a chemical one through changes in intermediary metabolism. Because of the interest of this laboratory in the possible role of the adrenal cortex in capillary permeability, it seemed wise to see if the adrenal cortical extract influenced the abnormal permeability induced by thermal trauma in the dog and at the same time to study its influence on the protein, carbohydrate and electrolyte changes of burn shock in the dog and in man.

It is to be recalled that at the time of this study two types of abnormal capillary permeability were believed to exist in burn shock: the first, that at the site of injury and the direct result of heat, had been demonstrated by Drinker and his co-workers,[5] while the second, a

4. Cope, O.; Brenizer, A. G., Jr., and Polderman, H.: Capillary Permeability and the Adrenal Cortex: Studies of Cervical Lymph in the Adrenalectomized Dog, Am. J. Physiol. **137**:69, 1942.

5. (*a*) Field, M. E.; Drinker, C. K., and White, J. C.: Lymph Pressures in Sterile Inflammation, J. Exper. Med. **56**:363, 1932. (*b*) Glenn, W. W. L.; Petersen, D. K., and Drinker, C. K.: The Flow of Lymph from Burned Tissue, with Particular Reference to the Effects of Fibrin Formation upon Lymph Drainage and Composition, Surgery **12**:685, 1942.

later peripheral increase in permeability as a result of diminished blood flow, had been postulated.[6] Since it was theoretically possible that the adrenal cortical hormone could affect either type of the abnormal permeability, a more extended survey of the nature of the abnormal permeability of burn shock was made.

In the initial experiments, capillary permeability was judged by observing in dogs the transfer of tagged molecules from blood stream to lymphatic vessel. These experiments have already been reported.[7] Radioactive isotopes in various chemical combinations were used as the tagged molecules. Abnormal capillary permeability was found only in traumatized or infected areas of the body; there was no evidence even in late shock of any generalized increase in permeability. Adrenal cortical extract was given to 3 animals; there was no demonstrable influence on the abnormal permeability in the burned area. The burns of the dogs' feet were severe, however (an immersion in boiling water for fifteen seconds), and because it seemed unreasonable to expect any hormone to exert an influence on necrosed capillaries, the observations were extended by determining the minimal amount of thermal trauma which would give reproducible alteration in capillary permeability and then, on such a preparation, the efficacy of adrenal cortical extract was tested. These experiments are reported in the present paper.

The idea of a controlling influence of extracts of the posterior lobe of the pituitary on the distribution of water within the body has been accepted. Although the posterior pituitary hormone acts on renal excretion of water and on peripheral blood flow, would it not be possible that this hormone might have a direct influence on capillary permeability?

In this paper are reported the effect of increasing temperature and duration of exposure on the capillary permeability of the dog's foot and the failure of adrenal cortical extract and posterior pituitary injection to influence either the abnormal permeability induced by even a minimal burn or the course of the protein, carbohydrate and electrolyte changes which follow a burn in the dog.

METHODS

Dogs weighing from 15 to 25 Kg. were used. They were maintained under pentobarbital sodium anesthesia throughout the experiment. A lymphatic trunk of each hindleg was cannulated above the ankle joint as described by Drinker and others.[5a] Burn trauma was produced by immersing the foot and ankle to the level

6. Moon, V. H.: Shock and Related Capillary Phenomena, New York, Oxford University Press, 1938.

7. Cope, O., and Moore, F. D.: A Study of Capillary Permeability in Experimental Burns and Burn Shock Using Radioactive Dyes in Blood and Lymph, J. Clin. Investigation **23**:241, 1944.

of the lymphatic cannula in water of known temperature for a specific time. The degree of trauma was judged by the change in lymph flow and in the concentration of the total and other proteins. The flow of lymph in these trunks is sluggish in the unburned resting dog under pentobarbital sodium anesthesia, and in order to obtain an adequate volume of lymph for control analysis it was usually necessary to stimulate the flow by gentle massage of the footpads. This massage was made as much as possible to simulate the pressure of walking in order to avoid mechanical

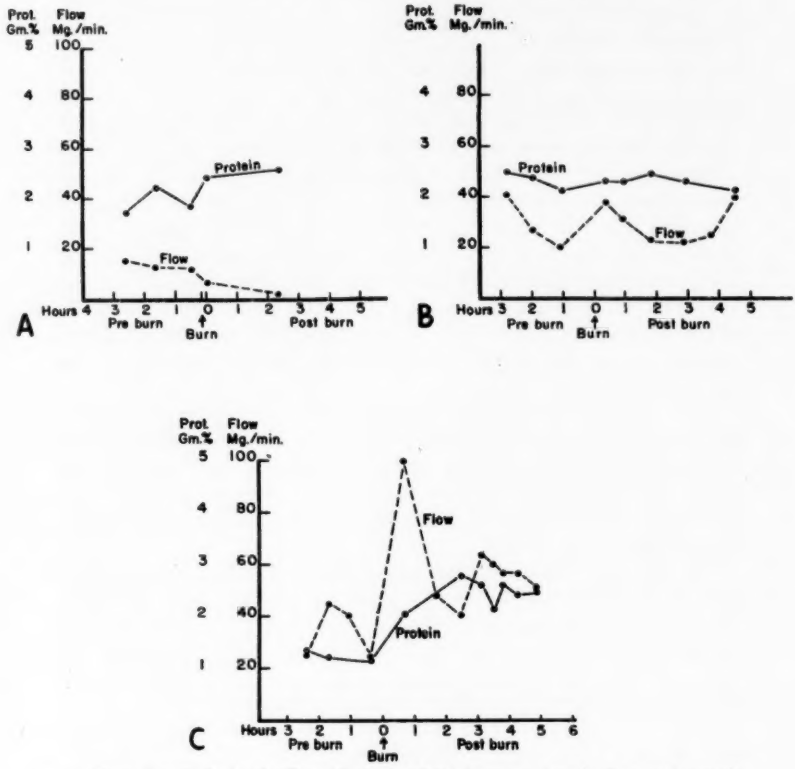


Chart 1.—*A*, lack of effect of subthreshold burn on lymph flow and protein concentration. The dog's foot was immersed in water at 60 C. for 10 seconds. *B*, increase in flow of lymph without change in protein concentration after subthreshold burn. The foot was immersed in water at 65.5 C. for 10 seconds. *C*, effect of threshold burn on lymph flow and protein concentration. Burn by water at 67 C. for 10 seconds. There is a significant rise in both flow and protein concentration.

trauma. After the trauma of a burn, the lymph flow is spontaneous; massage is not necessary and was not used. The amounts of lymph flow before and after burn are therefore not absolutely comparable, the amount recorded before burn being higher than the actual amount. The initial flow recorded before burn is further

increased above the actual amount by the transient obstruction incident to cannulation. The total protein concentration of lymph has been shown by Drinker to represent a measure of capillary permeability, provided the flow of lymph is maintained and the serum protein concentration is unaltered.

The mean arterial blood pressure was recorded periodically with a mercury manometer by puncturing the carotid artery with a needle, without interruption of the blood flow. All blood determinations were made on arterial blood taken from the carotid artery. The blood plasma, serum and lymph total protein levels were measured by the refractometer. In a number of the experiments these determinations were checked by the Kjeldahl method. When an albumin-globulin ratio is determined, when the nonprotein nitrogen is increased or when the plasma or lymph is fatty or hemolyzed, the refractometer protein value is always checked by the chemical method. Hematocrit values were determined on heparinized blood. Other chemical determinations were made by standard chemical methods.

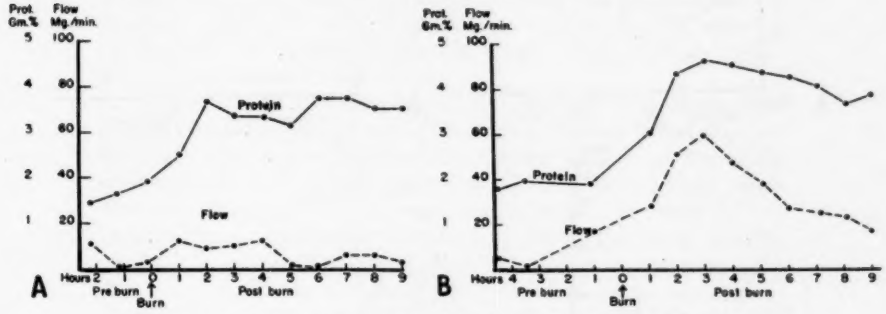


Chart 2.—*A*, the least effect of the minimal burn of water at 70 C. for 10 seconds. The protein concentration of the lymph rose to 3.5 Gm. per hundred cubic centimeters while the flow increased only perceptibly. *B*, the maximal effect of the minimal burn of water at 70 C. for 10 seconds. The protein concentration of the lymph rose to 4.5 Gm. per hundred cubic centimeters; the increase in the flow was moderate.

EXPERIMENTS

1. *Threshold of Burn Trauma.*—In this group of experiments the minimal burn of the dog's foot which would yield reproducible changes in lymph flow and total protein concentration was determined.

Little information was available to guide us. Drinker's observations, with one exception, had been made with the use of boiling water with an immersion period of two minutes, which produced a severe necrosing burn. In the exception, the temperature of the bath in which the dog's feet were constantly immersed was slowly raised; the first increase in lymph flow was recorded between 50 and 60 C.

After a control period of two to four hours during which control samples of lymph were collected for analysis, the dogs' feet and ankles

were submerged in water varying from 60 to 100 C. The immersion time chosen was ten seconds. Immersion in the 60 C. bath was followed by no significant alteration in lymph flow or total protein concentration (chart 1*A*). There was actually a drop in flow, but this is accounted for by cessation of massage. The slight rise in

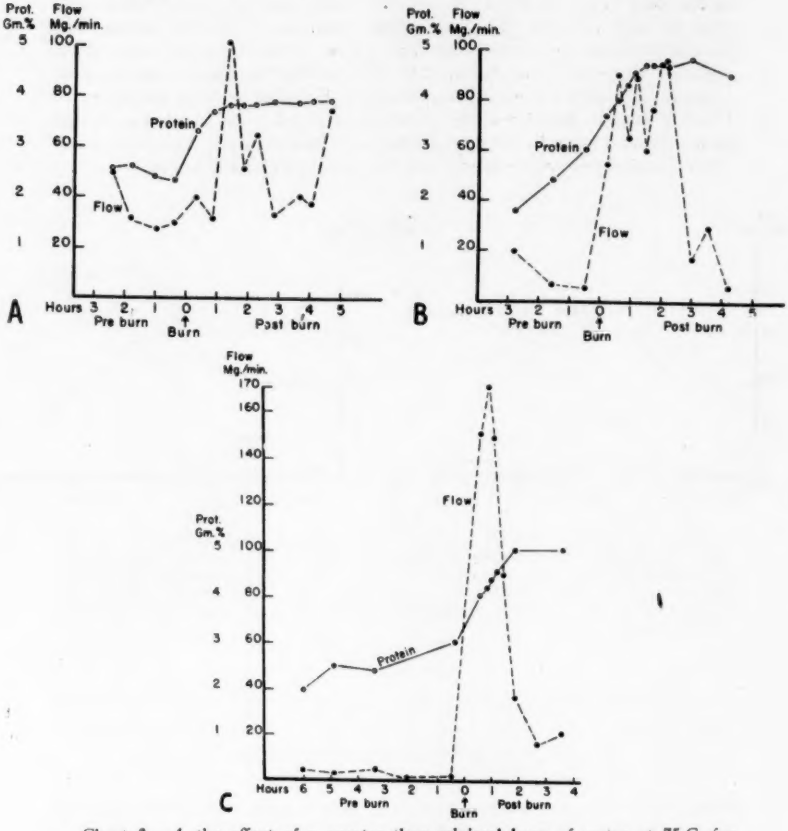


Chart 3.—*A*, the effect of a greater than minimal burn of water at 75 C. for 10 seconds. Although the change in protein concentration is no greater than that following a threshold burn, the rise in flow is. *B*, the effect of a moderate burn of water at 80 C. for 10 seconds. The rise both in protein concentration and in flow is significantly greater than that encountered after a mild or threshold burn. *C*, the effect of a severe burn of water at 100 C. for 20 seconds. The rise in protein concentration to 5 Gm. and of the flow to 170 mg. per minute within the first two hours after burn represent the maximal changes encountered.

protein concentration encountered is no greater than that to be expected after a period of massage.

After immersion at 65.5 C. there was a recognizable increase in the flow of the lymph (chart 1*B*). There was, however, no change in protein concentration. After immersion at 67 C. not only the lymph flow but also the protein concentration rose sharply from 1.2 to 2.5 Gm. (chart 1*C*): this is considered to constitute a threshold burn.

After immersion at 70 C. there was always a rise in both the flow and the protein concentration of the lymph, but the degree of rise was not consistent in the nine experiments carried out at this temperature. In chart 2*A* are shown the minimal rises and in chart 2*B* the maximal rises encountered. The rises in flow varied at their peaks from 12 to 62 mg. per minute, while the total protein concentration varied from 3.2 to 4.6 Gm. per hundred cubic centimeters. Because the changes were above the minimum observable and consistently present even though not consistent in degree, this temperature and duration of exposure were chosen as the standard for the assay of the hormones as possible therapeutic agents. The resulting injury constitutes a minimal burn.

Immersion at 75 C. and at 80 C. was followed by increasing rises in both lymph flow and protein concentration (chart 3 *A* and *B*). At 80 C. the total protein concentration reached 4.5 Gm. or above, the concentration found with the severe burns made with boiling water. The flow, however, was still below the maximal. In chart 3*C* are depicted the consequences of immersion at 100 C. for twenty seconds. There is an abrupt rise in both flow and protein concentration, the flow reaching 170 mg. per minute in an hour and the protein concentration 5.0 Gm. in two hours. These changes are maximal. In experiments with a more prolonged immersion time, neither lymph flow nor total protein concentration registered the increasing necrosis. Other changes, such as rate of edema formation and hemolysis in both lymph and serum, did reflect the increasing degree of tissue damage. The more prolonged the immersion in boiling water, the more rapid the tissue swelling.

Hemolysis was not observed following burns of 80 C. or less. The red pigment of hemolysis was grossly and consistently visible in the lymph after exposure to 100 C. for twenty seconds. With increasingly severe burns the intensity of hemolysis was augmented so that a burn at 100 C. for two minutes was immediately followed by a deep pink in the lymph draining from the burned area, and if two or more feet were burned there was delayed, grossly visible pigmentation of the blood plasma.

2. *Effect of Adrenal Cortical Extract on Permeability.*—The effect of adrenal cortical extract[8] on the abnormal capillary permeability

8. The Upjohn Company provided us with a generous supply of the aqueous extract of the cortex of the adrenal gland.

induced by a minimal burn was assayed in 8 dogs. The extract was administered within the first hour after the burn. Both hind feet and ankles of each dog were burned and the lymph changes of each wound recorded. The immersion temperatures were approximately 70 C. except for 3 feet immersed at 64.5, 68 and 73 C. The immersion time was ten seconds. No significant differences in lymph flow or protein concentration from those of the controls in this temperature range were observed. The findings in typical experiments are shown in chart 4.

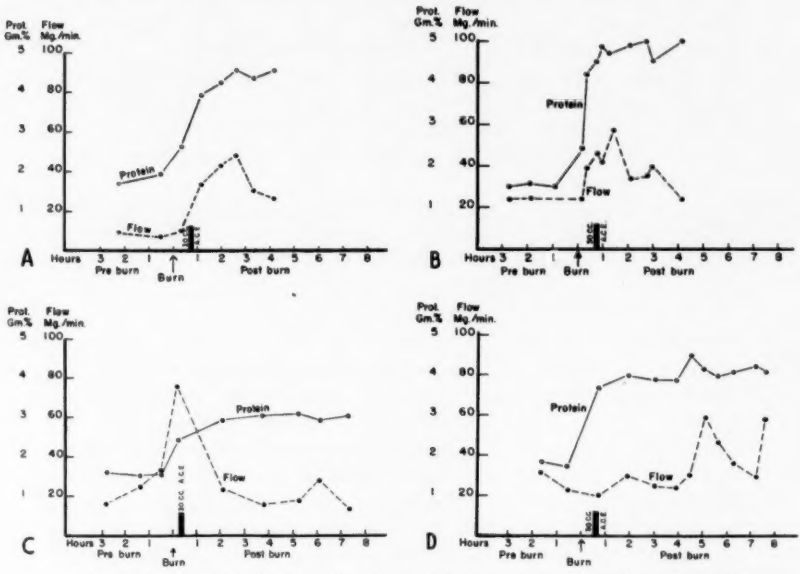


Chart 4.—*A*, lack of effect of adrenal cortical extract on lymph protein and flow after a threshold burn at 68 C. for 10 seconds. The changes observed are comparable to those encountered after a burn of similar severity in an untreated dog. *B*, lack of effect of adrenal cortical extract on the lymph flowing after a greater than minimal burn, 73 C. for 10 seconds. *C*, lack of effect of adrenal cortical extract on the lymph flow after a subthreshold burn, 64.5 C. for 10 seconds. *D*, lack of effect of adrenal cortical extract on the lymph flow after a minimal burn, 70.5 C. for 10 seconds.

3. *Effect of Posterior Pituitary Injection on Permeability.*—Extract of the posterior lobe of the pituitary gland (pitressin® [Parke, Davis & Co.]) was injected intravenously into 3 dogs whose hind feet and ankles had been burned by water at 70 C. for ten seconds. The first injection was given approximately one hour after the burn.

A second injection was given four to five hours later; the dog of the first experiment died immediately after this second injection.

The protein concentration of the lymph fell transitorily after the administration of the pituitary extract in four of the five observations. The fall was but 0.2 to 0.5 Gm. per hundred cubic centimeters and was apparent at one-half hour after the injection; at one and one-half hours after injection the concentration had returned to the preinjection level (chart 5). No such consistent change took place in lymph flow. From one-half of the wounds there was a decrease in flow starting

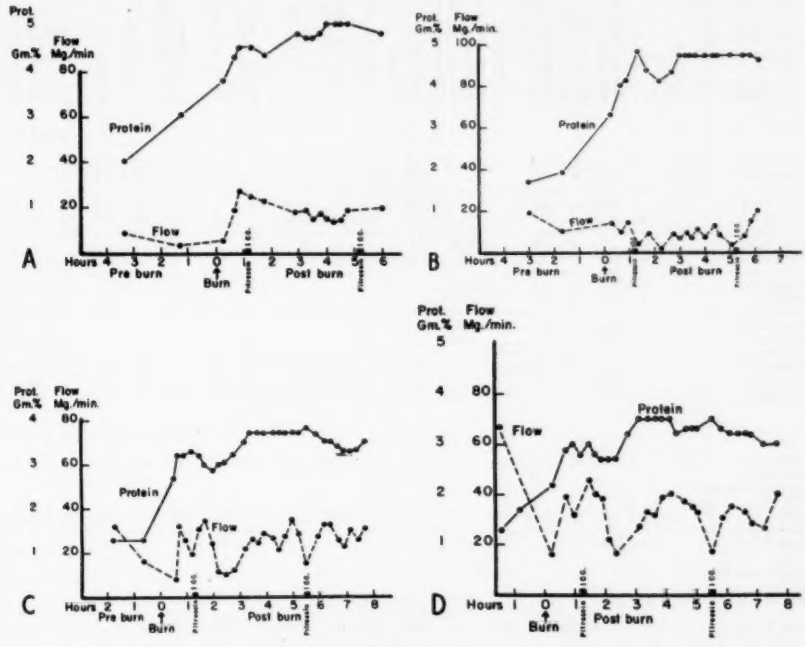


Chart 5.—*A*, effect of posterior pituitary extract on the lymph flowing after a minimal burn, 70 C. for ten seconds. There was a slight fall in the protein concentration immediately after the injection. *B*, effect of posterior pituitary extract on the lymph flowing after a minimal burn, 70 C. for ten seconds. The fall in protein concentration immediately after the injection was greater than that encountered in the experiment recorded in chart 5 *A*. *C*, effect of posterior pituitary extract on the lymph flowing after a minimal burn, 70 C. for ten seconds. After each injection there was a transient fall in protein concentration. *D*, effect of posterior pituitary extract on the lymph flowing after a minimal burn, 70 C. for ten seconds. The protein concentration is more irregular and the fall following each injection is less obvious than in the experiment recorded in chart 5 *C*.

one hour after injection, but after other injections there was a rise during the same period. The flow from the two feet of the same animal did not always change in parallel fashion.

Blood pressure changes were recorded throughout the experiments. In the first experiment the blood pressure was not followed during the injection, but it had fallen from 160 mm. of mercury before

TABLE 1.—A. *Chemical Observations on Blood*

Dog	Time	Hours	Blood Pressure, Mm. Hg.	Arterial Blood: Hematocrit Value, per Cent Cells	Arterial Blood: Serum: Total Protein, Gm. per 100 Cc.	Arterial Blood: Serum: A/G Ratio	Arterial Blood: Serum: Fibrinogen, Gm. per 100 Cc.	Arterial Blood: Serum: Amylase	Arterial Blood: Serum: Cholinesterase	Arterial Blood: Serum: Nonprotein Nitrogen, Mg. per 100 Cc.	Arterial Blood: Serum: CO_2, mEq. per Liter	Arterial Blood: Serum: Cl, mEq. per Liter	Arterial Blood: Serum: P, Mg. per 100 Cc.	Arterial Blood: Serum: Total Base, mEq. per Liter	Arterial Blood: Serum: Na, mEq. per Liter	Arterial Blood: Serum: K, mEq. per Liter	Arterial Blood: Serum: Ca, Mg. per 100 Cc.	Plasma Blood: Lactic Acid, Mg. per 100 Cc.	Plasma Blood: Pyruvic Acid, Mg. per 100 Cc.	Plasma Blood: Sugar, Mg. per 100 Cc.
A. Observations on																				
B 1	Before burn	..	...	47	7.1	...	....	11.2	10.5	25	25.0	114	3.2	155	144	3.9	5.7	....	...	100
	After burn	6	107	62	7.7	...	....	10.3	12.0	21	22.0	118	5.3	155	140	4.4	5.5	....	...	...
B 2	Before burn	..	143	40	6.7	...	....	13.7	....	74	24.9	117	...	152	140	3.8	5.6	....	...	99
	After burn	4	139	53	6.7	...	....	12.9	7.6	74	21.0	116	5.5	158	147	4.1	5.6	21.0	3.6	83
B11	Before burn	..	...	43	6.5	...	0.28	....	....	..	....	...	...	...	...	...	...	....	...	...
	After burn	3	148	51	7.1	...	0.34	....	....	..	....	...	...	...	...	...	...	....	...	...
B12	Before burn	..	136	45	6.3	...	0.27	....	....	..	....	...	...	...	...	...	...	....	...	...
	After burn	4	156	49	6.8	...	0.32	....	....	..	....	...	...	...	...	...	...	....	...	...
B13	Before burn	..	160	40	6.2	...	0.38	....	....	..	....	...	...	...	...	...	...	....	...	...
	After burn	4	186	52	6.9	...	0.39	....	....	..	....	...	...	...	...	...	...	....	...	...
B21	Before burn	..	180	47	6.3	1.5	....	18.3	10.5	96	19.2	108	6.6	...	136	2.8	5.0	11.3	2.9	192
	After burn	6	160	..	6.1	...	....	15.0	....	110	12.2	110	8.2	144	...	...	...	30.8	3.2	230
	After burn	21	60	74	7.5	0.6	....	17.4	12.9	177	12.6	106	13.7	160	137	...	4.7	80.4	5.3	210
B. Observations on Dogs Treated																				
B 9	Before burn	..	115	44	6.6	2.5	....	13.5	....	28	27.0	114	5.4	158	146	3.6	5.5	7.7	0.8	142
	After burn: Adrenal cortical extract	0.5+16																		
	After burn	28	161	65	5.8	3.5	....	9.5	....	104	13.9	110	8.4	158	146	5.6	5.1	40.0	3.6	161
B14	Before burn	..	195	43	6.4	...	0.51	....	....	..	....	...	...	...	...	...	...	....	...	...
	After burn: Adrenal cortical extract	0.5																		
	After burn	3.5	203	62	7.4	...	0.68	....	....	..	....	...	...	...	...	...	...	....	...	...
B20	Before burn	..	110	40	7.0	1.2	....	13.9	7.9	37	22.0	114	5.9	152	142	...	4.7	13.6	1.7	242
	After burn: Adrenal cortical extract	0.7																		
	After burn	6	95	47	7.8	1.1	....	11.7	....	31	23.3	110	7.2	152	...	...	...	8.4	2.2	154
	After burn	21	82	52	7.7	1.0	....	9.5	....	37	14.6	115	8.7	151	141	2.2	5.0	15.6	2.7	174
	After burn	24	68	49	7.3	1.1	....	9.6	....	57	12.1	115	9.9	147	138	2.4	5.1	21.7	2.6	170
	After burn	30	55	48	7.1	1.0	....	9.1	7.9	73	11.9	115	10.5	158	141	2.6	5.1	20.5	2.3	179
B24	Before burn	..	155	45	6.7	0.7	....	10.9	....	15	23.5	113	3.3	156	141	2.7	4.3	4.0	5.0	133
	After burn	5.5	56	60	7.0	0.6	....	9.1	....	15	18.3	121	4.3	164	140	...	4.2	8.7	1.4	171
	Adrenal cortical extract	18.5																		
	After burn	20	37	62	6.2	0.6	....	....	....	60	15.0	114	8.6	...	...	...	...	55.0	6.0	256
	Adrenal cortical extract	20.5																		
	After burn	21	...	63	6.3	0.6	....	8.2	....	73	13.7	99	11.1	162	139	10.6	4.3	65.0	4.0	286

injection to 150 mm. thirteen minutes after injection. At thirty-one minutes the blood pressure had returned to 156 mm. Immediately after the second injection, which was given rapidly, there was a pre-

cipitous decline from 140 to 26 mm., with death of the animal in five minutes. The four injections in the subsequent two experiments were given slowly over the course of at least one minute. The blood

Serum, Plasma and Lymph in Burned Dogs

Lymph																								
Leg									Cervical							Thoracic								
Total Protein, Gm. per 100 Cc.	A/G Ratio	Fibrinogen, Gm. per 100 Cc.	Amylase	Cholinesterase	Nonprotein Nitrogen, Mg. per 100 Cc.	Ca, Mg. per 100 Cc.	Cl, mEq. per Liter	Sugar, Mg. per 100 Cc.	Total Protein, Gm. per 100 Cc.	A/G Ratio	Amylase	Nonprotein Nitrogen, Mg. per 100 Cc.	Ca, Mg. per 100 Cc.	Cl, mEq. per Liter	Sugar, Mg. per 100 Cc.	Total Protein, Gm. per 100 Cc.	A/G Ratio	Amylase	Cholinesterase	Nonprotein Nitrogen, Mg. per 100 Cc.	Ca, Mg. per 100 Cc.	Cl, mEq. per Liter	Sugar, Mg. per 100 Cc.
Untreated Dogs																								
2.0	...	....	....	...	...	...	...	141	2.8	...	8.7	36	5.2	120	143	4.3	...	9.8	...	21	5.1	119	144
4.3	...	....	9.8	3.9	32	5.0	124	154	3.2	...	8.4	...	...	...	...	4.6	...	9.8	6.6	22	5.5	118	123
2.3	...	....	....	...	...	...	...	125	3.3	...	12.0	126	...	119	119	3.5	...	10.9	...	84	4.8	118	...
4.4	...	....	12.7	...	122	5.2	117	136	2.8	...	12.4	133	...	119	141	4.1	...	10.4	...	81	4.7	118	118
2.4	...	....	....	...	...	...	...	...	...	...	....	...	...	...	...	...	...	....	...	..	...	...	...
4.8	...	0.17	....	...	...	...	...	...	...	...	....	...	...	...	...	...	...	....	...	..	...	...	...
2.5	...	0.06	....	...	...	...	...	...	...	...	....	...	...	...	...	...	...	....	...	..	...	...	...
3.8	...	0.11	....	...	...	...	...	...	...	...	....	...	...	...	...	...	...	....	...	..	...	...	...
1.2	...	....	....	...	...	...	...	...	...	...	....	...	...	...	...	...	...	....	...	..	...	...	...
2.5	...	0.13	....	...	...	...	...	...	...	...	....	...	...	...	...	...	...	....	...	..	...	...	...
2.3	...	....	....	...	...	...	...	153	3.2	...	13.3	100	...	119	180	5.4	...	15.1	...	117	4.1	119	192
4.3	...	....	....	...	...	...	...	...	3.2	...	....	...	...	...	...	...	...	....	...	..	...	...	...
4.7	...	....	14.8	...	150	4.6	115	230	3.8	...	12.3	141	2.2	117	228	4.3	...	16.2	...	120	3.9	117	220
with Adrenal Cortical Extract																								
2.0	...	....	....	...	34	...	120	145	3.5	...	....	35	...	122	145	4.7	3.3	13.1	...	33	5.0	118	151
4.9	1.7	....	14.3	...	28	5.2	117	151	3.2	4.0	12.5	67	4.2	120	153	4.5	3.5	13.7	...	90	4.7	118	149
1.8	...	....	....	...	...	...	...	...	...	...	....	...	...	...	...	...	...	....	...	..	...	...	...
4.5	...	....	....	...	...	...	...	...	...	...	....	...	...	...	...	...	...	....	...	..	...	...	...
2.8	...	....	....	...	...	...	...	238	4.2	...	....	...	...	...	230	...	...	....	...	..	...	...	...
6.2	...	....	....	...	...	...	...	...	5.2	...	....	...	...	...	...	...	...	....	...	..	...	...	...
7.3	...	....	....	...	...	...	...	...	5.8	...	....	...	...	...	152	...	...	....	...	..	...	...	...
5.5	...	....	....	...	...	...	...	...	5.4	...	....	...	...	...	...	...	...	....	...	..	...	...	...
...	...	....	11.0	...	...	...	118	182	5.5	...	11.6	46	...	115	83	...	...	....	...	..	...	...	...
1.0	...	....	....	...	22	...	...	137	3.8	1.4	11.5	16	...	121	146	4.7	0.5	9.5	...	15	3.8	119	132
1.2	...	....	....	...	...	...	...	...	4.1	1.3	....	16	...	122	170	4.8	0.6	9.6	...	24	3.9	123	147
1.2	...	....	....	...	...	...	...	154	3.6	0.6	7.3	83	...	118	246	4.9	0.4	7.4	...	43	4.0	121	...
2.5	...	....	9.1	...	...	...	...	242	3.8	...	....	...	...	...	...	5.3	0.8	16.3	...	59	4.2	117	250

pressure was followed throughout each injection. In 1 dog (chart 5*A* and *B*) the blood pressure rose 5 and 17 mm. during the injections but fell to 100 and 13 mm. below the preinjection levels at fifteen

and twenty minutes after injection. There was a gradual return toward the preinjection level during the subsequent hour. In the other experiments (chart 5*C* and *D*), the blood pressure did not rise during the injections, but at fifteen minutes after the injections the pressure was 9 and 11 mm. higher than before, and it returned to the preinjection levels during the second fifteen minutes.

Respirations ceased during the first injection in the second experiment, but the animal survived after a short period of artificial respiration. In the final experiment the respirations were slowed by the first injection.

4. *Chemical Changes of Burn Shock and the Influence Thereon of Adrenal Cortical and Posterior Pituitary Extracts.*—A burn has long been known to be followed by changes in concentration within the extracellular fluid of the electrolytes, chlorides, sodium and potassium and of proteins in the plasma and to cause a rise in blood sugar.[9] The hormone of the adrenal cortex has been shown to influence the concentration and balance of these same electrolytes and carbohydrate metabolism.[10] The hormone of the posterior lobe of the pituitary gland not only causes retention of water but also affects carbohydrate metabolism.[11] An object was, therefore, to see to what extent the extracts of these two glands might influence the changes which follow a burn.

The changes in protein concentration of the plasma, the result of the loss of protein into the wound area, are reported elsewhere.[12] Comparable alterations in protein concentration of the serum were found in the dogs burned and treated with adrenal cortical extract (table 1). In three of the experiments with the adrenal cortical extract the amylase activity of the serum and cervical and thoracic lymphs was observed (table 1*B* B9, B20 and B24). Slight decreases were found in the activity in the serum and either an increase or no change in that of the lymph. In all cases the total protein concentration changed in the same direction. The changes in amylase activity and protein concentration were within the limits observed in the control animals, which were burned but not given extract.

9. Harkins, H. N.: The Treatment of Burns, Springfield, Ill., Charles C Thomas, 1942.

10. Swingle, W. W., and Remington, J. W.: The Role of the Adrenal Cortex in Physiological Processes, Physiol. Rev. **24**:89, 1944.

11. Burn, J. H.: The Modification of the Action of Iusulin by Pituitary Extract and Other Substances, J. Physiol. **57**:318, 1923.

12. Cope, O.; Graham, J. B.; Moore, F. D., and Ball, M. R.: The Nature of the Shift of Plasma Protein to the Extravascular Space Following Thermal Trauma, Ann. Surg. **128**:1041, 1948.

Cholinesterase activity was observed in the serum of 1 control and of 1 dog treated with cortical extract. There was a slight rise in activity in the control paralleling the rise in serum protein (B21). In the treated dog the activity did not change but the total protein fell from 7.6 to 7.1 Gm. (B20).

Changes in the albumin-globulin ratio after burning and differences in the ratio between blood and lymph were not consistent. The ratio in thoracic duct lymph tended to be higher than that in serum, as previously reported.[13] The fibrinogen content ran closely parallel to the total protein concentrations in both serum and lymph; there was thus no evidence of loss of fibrinogen in the wound area.

The effect of the pentobarbital sodium anesthesia was controlled in 3 animals (table 2). The changes in hematocrit value, serum pro-

TABLE 2.—*The Effect of Pentobarbital Sodium Anesthesia on the Hematocrit Value, Serum Total Protein and Nonprotein Nitrogen in Dogs*

			Arterial Blood		
				Serum	
Dog	Time	Hours	Hematocrit Value, % Cells	Protein, Gm./100 Cc.	NPN
NC1	After pentobarbital sodium	1.33	40	6.2	32
	After pentobarbital sodium	22	55	6.1	24
	After pentobarbital sodium	31.5	69	7.0	47
NC2	After pentobarbital sodium	1	41	6.7	61
	After pentobarbital sodium	10	57	6.7	34
	After pentobarbital sodium	20	49	6.6	42
	After pentobarbital sodium	26	43	5.9	37
ICN1	Before pentobarbital sodium	..	45	7.0	63
	After pentobarbital sodium	4.5	45	7.0	52
	After pentobarbital sodium	10	50	7.0	48
	After pentobarbital sodium	31.5	49	7.2	39
	After pentobarbital sodium	52	57	7.2	40

tein and nonprotein nitrogen were not consistent, but they may be interpreted as indicating slow, moderate dehydration.

The results of the total protein concentration, albumin-globulin ratio and enzyme activities are interpreted to mean that under the conditions of these experiments the adrenal cortical extract had no effect on the permeability of the capillary to these proteins.

The potassium and phosphorus concentrations rose in the extracellular fluid after the burn. There was no change in the serum and lymph sodium and serum chlorides. (The determinations in lymph of sodium, potassium, total base and phosphorus are not recorded in the tables because they were not significantly different from those of the serum.) The chloride and calcium content of the lymph from the leg after the burn fell and rose respectively in amounts to be expected

13. Drinker, C. K., and Yoffey, J. M.: Lymphatics, Lymph and Lymphoid Tissue, Cambridge, Mass., Harvard University Press, 1941.

from the rise in protein concentration. These changes are consistent with either a generalized cellular dehydration or release of these ions from the wounded cells. No significant difference was observed between the control animals and those treated with cortical extract.

The burn was followed by a sharp rise in lactic and pyruvic acid levels of the blood plasma (table 1). Comparable levels were found in the various lymphs whenever measured and are therefore not recorded. The blood and lymph sugar levels, increased after administration of pentobarbital sodium, remained increased or rose further after the

TABLE 3.—*The Chemical Observations in Blood Serum, Plasma and Lymph in Burned Dogs Treated with Posterior Pituitary Extract*

			Arterial Blood													Leg Lymph	
					Serum							Plasma					
Dog	Time	Hours	Blood Pressure, Mm. Hg.	Hematocrit Value, per Cent Cells	Protein, Gm./100 Cc.	pH	CO_2, mEq./Liter	Cl, mEq./Liter	P, Mg./100 Cc.	Total Base, mEq./Liter	Na, mEq./Liter	K, mEq./Liter	Lactic Acid	Pyruvic Acid	Blood Sugar, Mg./100 Cc.	Total Protein, Gm./100 Cc.	pH	CO_2, mEq./Liter
B 25	Before burn	..	164	37.7	5.9	7.38	28.0	115	3.9	157	149	3.6	5.2	0.9	152	...	7.59	30.0
	After burn	0.8	150	38.7	...	....	....	...	...	152	...	...	...	...	152	...	7.60	27.4
	Posterior pituitary extract	1																
	After burn	2	150	40.5	6.1	7.35	25.6	114	4.4	158	143	4.7	17.0	2.3	139	...	....	....
	After burn	3	160	40.3	6.1	7.39	26.9	114	4.1	157	143	4.0	6.8	5.0	159	...	7.50	27.5
B 26	Before burn	..	150	43.6	7.9	7.55	....	...	...	...	...	...	...	...	...	1.9	7.66	....
	After burn	1	145	46.5	7.9	7.57	....	...	...	...	...	...	...	...	...	...	7.61	....
	Posterior pituitary extract	1																
	After burn	3	140	51.0	8.1	7.25	....	...	...	...	...	...	...	...	...	4.5	7.61	....
B 27	Before burn	..	120	39.4	6.5	7.39	....	...	5.7	...	...	...	5.5	0.8	135	1.7	7.37	....
	After burn	1	124	42.3	6.8	7.35	....	...	4.7	...	...	...	6.0	0.9	147	2.8	7.37	....
	Posterior pituitary extract	1																
	After burn	2	116	47.5	6.8	7.25	....	...	4.7	...	...	...	11.6	0.2	148	3.2	7.37	....
	After burn	4	117	47.2	7.0	7.27	....	...	5.6	...	...	...	5.6	0.8	139	3.2	7.38	....
	Posterior pituitary extract	6																
	After burn	10	118	50.0	7.2	7.30	....	...	4.6	...	...	...	5.5	1.3	150	3.0	7.37	....

burning. There were no differences between the control animals and those treated with cortical extract. In 3 animals the effect of pituitary extract was observed (table 3). With the dosage employed, there was no significant difference from the controls (table 1 *A*).

COMMENT

The thesis on which these experiments were undertaken, that the extract of the adrenal cortex is beneficial in burn shock, is not substantiated. Neither a sparing action on the loss of plasma into a burn wound nor a reversal of the pattern of electrolyte and metabolic change was found. Loss of plasma stems from increased permeability of the capil-

laries of the wound, and no effect on this increased permeability was observed. The beneficial action of substitution therapy in the adrenalectomized, cortically insufficient animal was not duplicated in the burned animal even though the abnormal electrolyte pattern of the extracellular fluid of the 2 animals is similar.

The negative findings in these experiments with adrenal cortical extract are not to be construed to mean that the cortical hormone is without influence on capillary permeability or that it does not sway the course of shock following burns by some as yet hidden metabolic effect. It is clear from Selye's description of the adaptation reaction that the adrenal cortex is stimulated to overactivity by trauma.[14] Hypersecretion of the adrenal cortex in the human being as part of the reaction to a burn has been amply proved.[15] Just what this response of the adrenal cortex means to the organism, however, is still obscure, and it is undetermined whether heightened cortical function from the administration of extract is desirable. It is certain that adrenal cortical extract should not be given to an extensively burned patient with the idea that it will diminish the amount of plasma or water loss or the need for protein, electrolyte and fluid therapy.

The experiments with posterior pituitary extract also point to no beneficial effect to be obtained in burn shock from the use of this hormone. Under the conditions of the experiments, no action on the abnormal capillary permeability of the burn wound was demonstrated. The transitory drop in protein concentration of the lymph flowing from the wound after administration of posterior pituitary extract should not lead to the use of this hormone in an effort to decrease loss of plasma; the drop is more likely to be due to a decrease in arteriolar blood flow and capillary pressure than to a change in capillary permeability. The arteriolar constriction presumably is not limited to the burn wound, and indeed fatal constriction of the coronary artery has been described. To advise against the use of posterior pituitary hormone in burn shock, however, is not stating that the posterior lobe of the pituitary is not called on for extraordinary secretion during the dehydration phase of burn shock.

---

14. Selye, H.: The General Adaptation Syndrome and the Diseases of Adaptation, J. Clin. Endocrinology **6**:117, 1946.

15. Browne, J. S. L.: Personal communication to the author, 1942. Cope, O.; Nathanson, I. T.; Rourke, G. M., and Wilson, H.: Symposium on the Management of the Cocoanut Grove Burns at the Massachusetts General Hospital: Metabolic Observations, Ann. Surg. **117**:937, 1943. Shipley, R. A.; Dorfman, R. I.; Buchwald, E., and Ross, E.: The Effect of Infection and Trauma on the Excretion of Urinary Cortin, J. Clin. Investigation **25**:673, 1946. Talbot, N. B.; Nathanson, I. T., and Cope, O.: Unpublished Data.

SUMMARY

The efficacy of extracts of the adrenal cortex and posterior lobe of the pituitary gland in the treatment of burn shock has been tested in the anesthetized dog; the test objects used were the increased capillary permeability in the burned foot and the changes in intermediary metabolism of protein, carbohydrate and electrolytes induced by the burn.

The threshold of burn trauma which registers as an increase in flow and protein concentration of the lymph draining from the burned foot of the dog was found to be an immersion for ten seconds in hot water of 67 C. Minimal and consistent increases were produced by immersion for ten seconds in water of 70 C. Burns of greater severity are followed by more precipitous and higher rises in lymph flow and protein concentration, more rapid edema formation and hemolysis.

The possible influence of the glandular extracts on the increased capillary permeability was tested on threshold and minimal burns. No effect of the adrenal cortical extract was demonstrable. The use of posterior pituitary extract was followed by a slight, transitory drop in protein concentration of the lymph.

The changes in intermediary metabolism observed following burns were also not influenced by the gland extracts.

No evidence was obtained to substantiate the concepts that these gland extracts are useful in the treatment of burn shock.

EFFECT OF THERAPEUTIC COLD ON THE CIRCULATION OF BLOOD AND LYMPH IN THERMAL BURNS

An Experimental Study

JOHN L. LANGOHR, M.D.
LEON ROSENFELD, M.D.
CORA R. OWEN, Ph.D.
AND
OLIVER COPE, M.D.
BOSTON

A CHILD soon learns that cold relieves the pain of a burn, and cold has been used since ancient times in the treatment of burns. More recently, at the beginning of the second World War, Webster and others [1] and White and his associates [2] recommended cold in the therapy of immersion foot. They found not only that it relieved the pain but also that it was followed by some reduction in volume of the edema. Should such reduction in edema be achieved in a burn the use of cold might materially reduce the volume of plasma needed in the therapy of burn shock.

There are also theoretic reasons pointing to the use of cold for burns. Cold should diminish the metabolic demands of the wound, and if the circulation to the wound were impaired, the degree of tissue damage might be decreased. Bacterial infection should be reduced by the established effect of cold in decreasing bacterial growth.

This work was aided by a grant from the Ciba Pharmaceutical Products, Inc., Summit, N. J.

From the Surgical Research Laboratories of the Harvard Medical School at the Massachusetts General Hospital.

The work described in this paper was done under a contract, recommended by the Committee on Medical Research, between the Office of Scientific Research and Development and Harvard University.

1. Webster, D. R.; Woolhouse, F. M., and Johnston, J. L.: Immersion Foot, J. Bone & Joint Surg. **24**:785, 1942.

2. White, J. C.: Vascular and Neurologic Lesions in Survivors of Shipwreck: Immersion-Foot Syndrome Following Exposure to Cold, New England J. Med. **228**:211, 1943. White, J. C., and Scoville, W. B.: Trench Foot and Immersion Foot, New England J. Med. **232**:415, 1945.

In addition, Drinker and others [3] have stressed the fact that edema may retard the healing of burn wounds; Blalock [4] has reported an increase in survival time of the dog traumatized with a crushing clamp and treated with cold, and F. M. Allen [5] has recommended enthusiastically the use of cold for all forms of trauma. For all these reasons, theoretic and reported, a probe into the rationale for the use of cold in cases of burns was started. The initial experiments observing lymph flow and edema formation were sufficiently suggestive for the experimental program to be extended to include measurement of the arterial circulation.

METHODS

Male dogs in good health weighing from 18 to 22 Kg. were chosen for the experiments. In all, 19 dogs were used. Pentobarbital sodium was administered intravenously or intraperitoneally for anesthesia. The skin of both hindlegs and that overlying a carotid artery was prepared by clipping the hair and applying diluted tincture of iodine and alcohol. The operations were performed under aseptic precautions to avoid as much clostridial infection as possible.

The lymphatic trunks running on either side of the vein of both hindlegs were exposed above the ankle; one was cannulated, and the flow of lymph in the other was diverted to the cannula by closing it with a ligature. The flow of lymph was generally so sluggish before the foot was injured that gentle massage to the foot pads was necessary in order to secure sufficient lymph for control analysis. After injury spontaneous flow only was collected. The flow was measured by weight and recorded in milligrams per minute. Powdered heparin was inserted into the open end of the cannula periodically by means of a fine wire to prevent coagulation of lymph protein.

The arterial blood flow into the foot was measured by means of a U tube flow meter inserted into the anterior tibial artery of each hindleg above the ankle (fig. 1). The anterior tibial rather than the femoral artery was used in order to limit the measurement of blood flow as much as possible to that flowing to the tissues to be damaged. The posterior tibial artery was not ligated.

In order to avoid undue loss of blood during the operations heparinization was delayed until the anterior tibial arteries had been isolated and a blood pressure cannula inserted in the carotid artery. Infusion of heparin [6] by continuous drip into a vein in the front of the leg was carried out.

---

3. Glenn, W. W. L.; Petersen, D. K., and Drinker, C. K.: The Flow of Lymph from Burned Tissue, with Particular Reference to the Effects of Fibrin Formation Upon Lymph Damage and Composition, Surgery **12**:685, 1942. Glenn, W. W. L.; Gilbert, H. H., and Drinker, C. K.: The Treatment of Burns by the Closed Plaster Method, with Certain Physiological Considerations Implicit in the Success of This Technique, J. Clin. Investigation **22**:609, 1943.

4. Blalock, A.: A Comparison of the Effects of the Local Application of Heat and of Cold in the Prevention and Treatment of Experimental Traumatic Shock, Surgery **11**:356, 1942.

5. Allen, F. M.: Reduced Temperatures in Surgery: III. Experiments on Pelvic and Abdominal Refrigeration with Especial Reference to Traumatic and Military Surgery, Am. J. Surg. **55**:451, 1942.

6. The heparin (liquaemin®) was supplied through the generosity of Roche Organon, Inc., of Nutley, N. J.

The anterior tibial arteries were then opened, a glass cannula inserted in each proximal and distal opening and the flowmeters connected to them. The flowmeters (fig. 1) were of the same type as those used in the experiments testing the effect of a restrictive plaster dressing on a burn wound.[7] Blood flow was observed until stable. All readings were made at systole during expiration; each recording was an average of three readings.

The flowmeters were calibrated at the end of each experiment with blood removed from the dog at that time. Although the actual flow through the meter

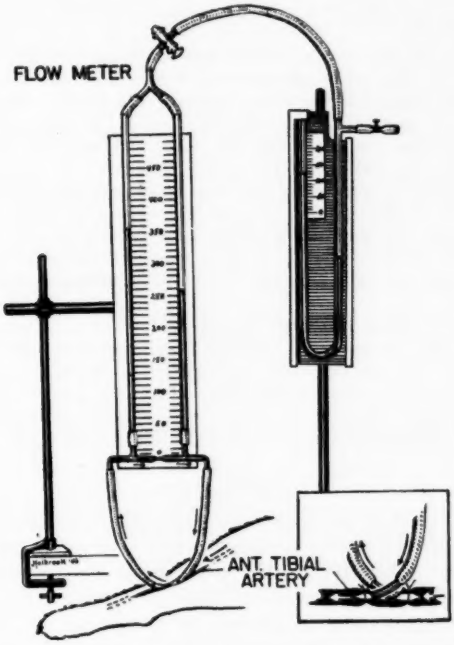


Fig. 1.—Arrangement of U tube flow meter attached to mercury manometer to measure blood pressure. Inset shows glass cannulas inserted into anterior tibial artery of hindleg of dog and connected to flowmeter by means of short segments of rubber tubing. Arrows show direction of blood flow.

during the experiment was thus determined, the amount was presumably not the same as it would have been had the arteries been intact. The presence of the cannulas and the meter inevitably resulted in some obstruction to flow. This factor of obstruction must be kept in mind when interpreting the observations. In spite of

7. See article in this issue entitled "Explorations Into the Physiologic Basis for the Therapeutic Use of Restrictive Bandages in Thermal Trauma: An Experimental Study," page 1056.

the limitation of partial obstruction, the sensitivity of the apparatus to change in blood flow is beyond question.

The sensitivity of the apparatus to change in blood flow was established by control experiments. In several of the experiments, before the feet were subjected to damaging heat the blood flow was measured with the foot immersed in water of 10 C.; a reduction in flow was recorded. Immersion at 40 C. resulted in prompt increase in flow. At the end of one experiment, spinal anesthesia was induced with procaine hydrochloride; a prompt increase in flow took place.

The mean arterial pressure of the blood flow to the wound was measured in the anterior tibal artery by connecting the tops of the U tube with a mercury manometer (fig. 1); it was also recorded in the systemic circulation through the cannula in the carotid artery.

The infusion of heparin was continued intermittently by slow drip throughout the experiment. Because of the heparinization, sufficient blood oozed from the tibial arterial wounds in the majority of the experiments to warrant returning it to the circulation. The oozing blood was collected in a pan, periodically filtered, diluted with isotonic sodium chloride solution and slowly injected intravenously.

The trauma was inflicted by dipping both hindfeet to an identical level just below the ankle in a deep pan of hot water. Temperatures of the water varied from 80 to 100 C.; the duration of immersion was ten or fifteen seconds. Cold used in treatment was applied by a similar water bath technic, the temperature of the water being 10 C. The bath of water insured the application of a uniform temperature and rate of conduction. The bath temperatures were maintained within 1 C.

The degree of edema in both the injured and the uninjured feet in the experiments using cold as treatment was recorded as the increase in width of the feet in millimeters. In the experiments studying the effect of intravenous infusions on the rate of edema formation, a plethysmograph was used for greater accuracy.[7]

The blood plasma and lymph proteins were measured by the refractometer. The chemical measurements were made by standard analytic methods.

OBSERVATIONS

The effect of cold on the abnormal circulation of blood and lymph and on the rate of edema formation induced by a thermal burn was studied in the feet of dogs. The experiments are grouped according to which circulation was measured and into control groups testing the effects of the treatment bath and of a rapid intravenous infusion on edema formation.

Effect of Cold on Lymph Circulation of the Burned Foot.—The effect of cold on the increased flow and protein concentration of lymph from a burned foot of a dog was observed in three experiments (figs. 2, 3 and 4). In a previous publication [8] it was established that the minimal burn of a dog's foot producing a consistent rise in lymph flow and protein concentration was one caused by immersion in water at 70 C. for ten seconds. Such a minimal burn was chosen to test the response

8. See article in this issue entitled "Threshold of Thermal Trauma and Influence of Adrenal Cortical and Posterior Pituitary Extracts on the Capillary and Chemical Changes: An Experimental Study," page 1015.

to therapeutic cold. The temperature selected for the cold bath was 10 C., based on the experience of Sir Thomas Lewis, who showed that the human skin survived, undamaged, immersion at this temperature.[9] (The absence of effect of this temperature on lymph flow and protein concentration in the dog is demonstrated in the control experiments described later.)

Under pentobarbital sodium anesthesia and without heparin infusion, the lymphatic vessels of both hind legs were cannulated. Control samples of lymph were collected after gentle massage and the size of the feet observed before the burning. In the first and second experiments both feet were burned and in the third only one. In the first experiment one foot was placed immediately after burning in the cold bath, where it was kept for three and a half hours. There was a slight spontaneous flow of lymph into the cannula while the foot was

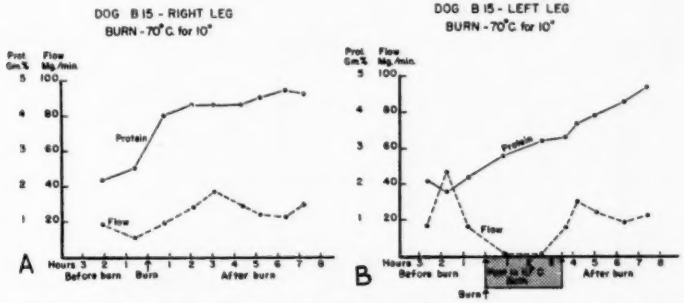


Fig. 2.—Effect of cold on lymph flow and protein concentration from a minimal burn of the hindfeet of dog B15. The burn was produced by immersion in water of 70 C. for ten seconds. *A*, the control leg; *B*, the cold-treated leg (10 C. for three and a half hours).

in the cold water, but on its removal from the cold to room atmosphere there was a prompt rise in flow (fig. 2*B*), comparable to that encountered soon after injury in the opposite, untreated leg (fig. 2*A*)

After injury the rise in protein concentration in the lymph from the foot burned but not treated with cold was prompt and in the concentration reached, 4.5 Gm. per hundred cubic centimeters, was typical of the change following a thermal injury of like severity (fig. 2*A*). The rise in protein concentration in the lymph from the treated foot was gradual. After withdrawal from the cold there was a further rise to the level of the untreated foot (fig. 2*B*).

9. Lewis, T.: Observations on Some Normal and Injurious Effects of Cold Upon the Skin and Underlying Tissues: I. Reactions to Cold, and Injury of Normal Skin, Brit. M. J. **2**:795, 1941.

While the treated foot was in the cold bath, there was but barely visible swelling. After withdrawal, edema formed promptly, the size of the foot reaching that of the untreated foot within two hours. The untreated foot had swelled promptly after injury.

In the second experiment the foot was not immersed in the cold water until one and a quarter hours after the burn (fig. 3*B*). In the interval between burn and immersion, lymph flow, protein concentration and edema had increased comparably in both feet. After immersion in the cold, the flow of lymph was sharply reduced, but it did not cease while in the cold. The amount of edema, however, was visibly reduced by the end of the immersion in cold. On withdrawal of the foot from the cold the increased rate of lymph flow and edema formation was resumed. The protein concentration was reduced

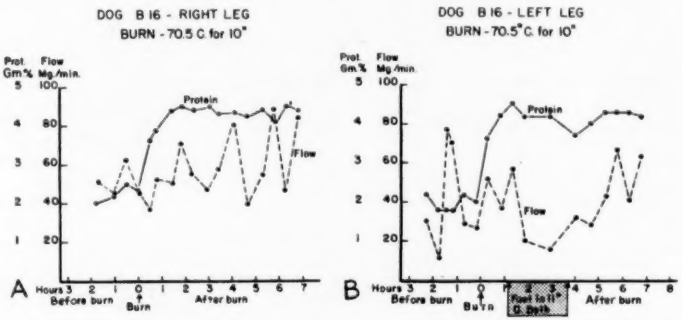


Fig. 3.—Effect of cold on lymph flowing from a minimal burn, 70.5 C. for ten seconds, in dog B16. The immersion in the cold bath (11 C.) was delayed until one and one quarter hours after burning. *A*, the control leg; *B*, the cold-treated leg.

slightly during immersion in cold and promptly rose again on withdrawal. The continued lymph flow during the immersion in this experiment was apparently in part at the expense of the edema fluid which had accumulated in the interval between injury and immersion in cold.

In the third experiment both a burned and an unburned foot were placed in the cold bath. The influence of the cold on the burned foot (fig. 4*A*) was comparable to that in the first experiment. There was no effect on the lymphatic circulation of the unburned foot produced by exposure for two hours and forty minutes (fig. 4*B*).

Effect of Cold on Arterial and Lymph Circulation of the Burned Foot.—In ten experiments both the arterial and the lymphatic circulations were measured.

The hematocrit value was measured at the time of heparinization. A control sample of lymph was obtained from the two feet. A period of stable blood flow for one to three hours was recorded. After the preburn width had been recorded, the hindfeet were burned in 4 dogs at 80 C., 5 at 90 C. and 1 at 100 C., all for fifteen seconds. Immediately after the burn, the hindfoot to be treated with cold was immersed in the water bath at 10 C., the immersion lasting for two and a half to six hours. The control hindfoot, hanging down from the table at the same level as the treated foot, was exposed to the room air. Neither the intensity of the burn nor the duration of the immersion in the cold bath altered the pattern of response. The findings in two typical experiments are given in figure 5.

A sequence of changes in the circulation of the skin and in the development of edema of the wound were visible as the result of the

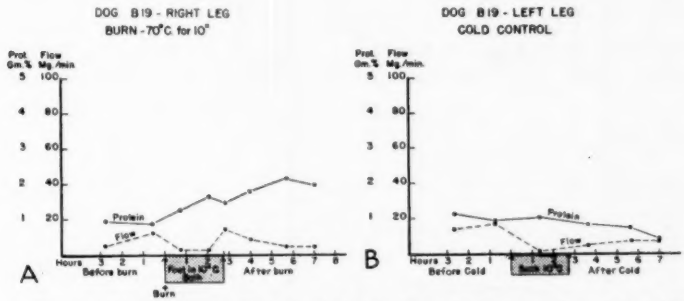


Fig. 4.—Comparison of effect of cold on the burned (*A*) and unburned foot (*B*) of dog B19. The burn was produced by an immersion at 70 C. for ten seconds and the chilling by a bath of 10 C. for two hours and forty minutes.

trauma and treatment. Immediately on immersion of the foot in the hot water, there was blanching, which was followed within a few seconds by a flush. On withdrawal, the flush of the untreated control foot continued, gradually changing to cyanosis. The foot swelled, and blebs formed between the toes.

The foot treated with the cold swelled but little and slowly while in the bath; no blebs appeared. On its withdrawal from the cold, the rate of edema formation was abruptly accelerated and blebs appeared (see bottom section of figure 5).

No consistent change in blood pressure, measured in the tibial artery, was noted as the immediate result of injury or therapy. In some experiments the pressure rose slightly on immersion of the foot in the hot water (fig. 5*A*); in others there was either a slight drop (fig. 5*B*) or no change. No changes were established as the result

of withdrawal from the hot water or of the immersion in cold. During the course of the experiment there were fluctuations in pressure in all animals, influenced by supplementary injections of pentobarbital sodium in some instances, and there was a general downward course of the pressure in some experiments (fig. 5*B*) and no change in others (fig. 5*A*). In all the experiments included, the condition of the animal

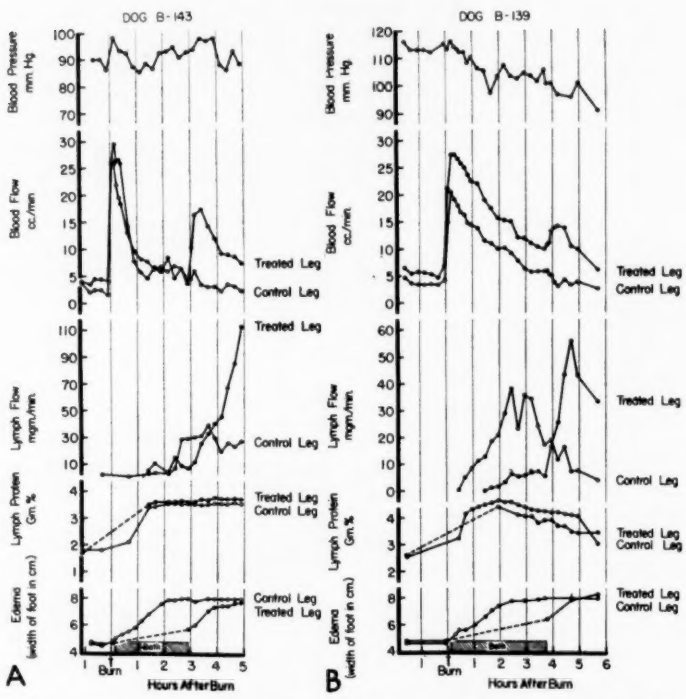


Fig. 5.—*A*, effect of a burn and cold treatment on the arterial and lymphatic circulation and edema formation in dog B143. The burn was produced by an immersion at 80 C. for fifteen seconds and the chilling by immersion at 10 C. for two and three quarters hours. The recorded blood pressure was measured by the tibial artery flowmeter. *B*, effect of a burn and cold treatment on the arterial and lymphatic circulations and edema formation in dog B139. The burn was at 90 C. for fifteen seconds and the chilling at 10 C. for three and three quarters hours. The recorded blood pressure was of the tibial artery.

was considered satisfactory, blood flow being maintained and the arterial pressure at no time below 85 mm. of mercury.

Striking alterations of blood flow were consistently encountered immediately after the burn and in the treated foot after withdrawal

from the cold bath. In all experiments there was an abrupt immediate rise in flow when the feet were immersed in the hot water, the extent of the rise being independent of the temperature within the range of temperature used. Removal from the water was followed by a fall in flow, abrupt initially in some experiments and gradual in others. This fall was not influenced by the immersion in cold water. In the untreated leg the flow returned to the preburn rate in three to four hours.

In the treated leg there was a second abrupt rise in flow on withdrawal from the cold bath. This rise was not to as high a level as that reached immediately after the burn, but it was sustained for from forty minutes to one and a half hours. Thereafter the flow declined to the preburn level. In the foot not exposed to cold there was no consistent change in flow at the time when the treated foot was removed from the cold bath. In some experiments there was either a slight fall, a rise or no recognizable change. This difference in flow pattern of the two feet on cessation of cold therapy indicated that the second rise in rate of flow in the treated leg is the result of a reflex, locally governed.

The pattern of flow and protein concentration of lymph from the burned foot immersed in the cold bath was comparable to that of the first group of experiments. During the exposure to cold, the flow of lymph and the development of edema were retarded. The more severe the injury, the more exaggerated the difference in flow between the treated and the control foot. On removal from the cold bath, the rate of flow increased rapidly and subsequently decreased when the edema of the treated foot had reached its maximum, an amount comparable to that of the control foot, which had been reached two hours after injury (fig. 5).

The rise in protein concentration in the lymph of the control foot was typical of that following thermal trauma. The protein concentration also rose in the lymph from the treated foot during the application of the cold. As soon as the volume of lymph was sufficient for measurement, in some experiments the concentration was found already to have reached or exceeded that of the lymph from the control foot. In other experiments the concentration in the lymph from the treated foot remained below that in the lymph from the control foot throughout the period of exposure to cold.

It is to be noted at this point that the pattern of lymph flow is altered by the cold throughout the period of immersion of the foot; in contrast, the arterial blood flow is not influenced until removal of the foot from the cold, and then only is the blood flow different in the two feet.

In conformity with the previously reported observations, the lymph in the initial period after a burn at 90 or 100 C. showed slight hemolysis.

In the burned foot not immersed in the cold bath the maximum edema is reached two to two and a half hours after the burn. In the treated foot the rate of edema formation is much lower than in the control foot, but it is not negligible during the period of treatment. This rate is not consistent in all experiments. In the period immediately following withdrawal from the cold bath there is a prompt increase in the rate of edema formation. In experiments in which the bath was continued for only three to four hours, the edema eventually reached the volume present in the control feet. In the experiment in which immersion lasted for six hours, edema ceased to form before the size of the foot reached that of the control foot while in the bath. After withdrawal, although the edema increased a little, the size never reached that of the control foot.

Effect of Cold on Lymph Circulation of the Unburned Foot.—Because it was observed in the first group of experiments that the flow and the protein concentration of the lymph from an unburned foot were unaltered by an immersion at 10 C. for two hours and forty minutes (fig. 4*B*), it was considered wise to test at a lower temperature to make sure that the immersion itself did not damage the capillary bed.

After cannulation of the lymphatic trunk, one foot of each of two animals was immersed for three and three and three-quarter hours, respectively, in water at 0 C. and the lymph flow and protein concentration observed for several hours thereafter (fig. 6*A* and *B*). In the experiment with the immersion lasting for three hours (fig. 6*A*), there was initially no flow, but after immersion there was a moderate spontaneous flow that was still rising when the experiment was ended. The protein concentration after immersion was nearly one gram lower than during the period of massage before immersion. In the experiment with the immersion lasting three and three-quarter hours (fig. 6*B*) there was a slight spontaneous flow after removal from the bath and, as in the previous experiment, a fall in protein concentration. The failure of the protein concentration to rise excluded a bath of this temperature and duration as the cause of any of the changes recorded in the experiments on treatment.

Effect of Intravenous Infusion.—The effect of a rapid intravenous infusion of isotonic sodium chloride and sodium lactate solutions on rate and degree of edema formation was studied in four experiments. The volume of the four feet of each animal was measured in separate plethysmometers. One forefoot and one hindfoot were burned at 90 C. for fifteen seconds, a burn of medium severity known to produce a consistent curve of edema formation with minimal loss of elasticity

of the skin. Experience has indicated that nearly maximum edema is produced by such a burn, the peak of the edema having been reached between the second and third hours after injury.

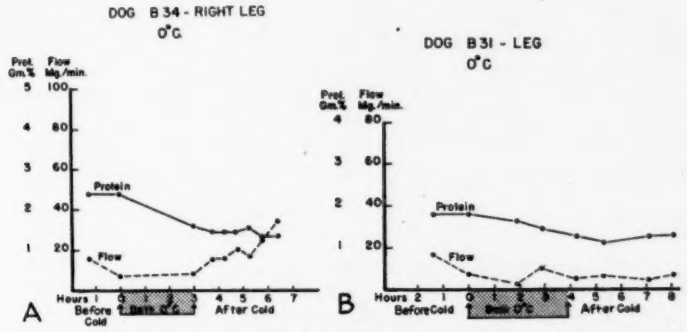


Fig. 6.—*A*, effect of cold on the flow and protein concentration of lymph in right leg of dog B34. The immersion at 0 C. for three hours was followed by an increase in flow but not of protein cencentration. *B*, effect of cold on the flow and protein concentration of lymph in right leg of dog B31. The immersion at 0 C. for three hours was followed by slight spontaneous flow and a gradual fall in protein concentration.

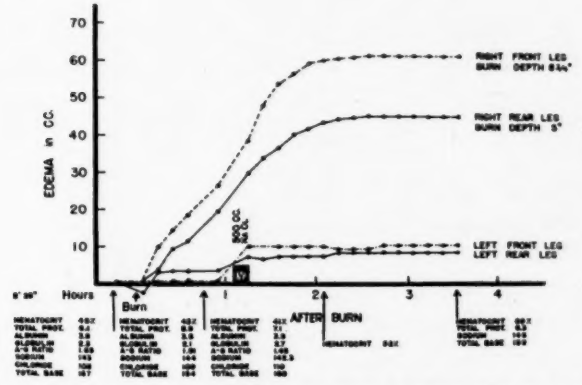


Fig. 7.—Effect of intravenous infusion on rate and degree of edema formation following a burn at 90 C. for fifteen seconds in dog B121. Infusion of 500 cc. of isotonic sodium chloride was begun seventy minutes after injury. There was a rise in the rate of edema formation in the burned feet as well as a slight increase in the volumes of the uninjured feet.

In the first experiment an infusion of 500 cc. of sodium chloride was given in a twelve minute period starting at the seventieth minute

after the burn. An increase in the rate of edema formation in the injured feet was apparent immediately after the infusion (fig. 7). There was also a slight increase in the volumes in the uninjured feet, which indicated an expansion of the entire extracellular space.

In a second experiment the infusion of 400 cc. of isotonic sodium lactate solution was not started until the end of the fourth hour after the burn and one hour after the volume of edema had ceased to increase in both injured feet. Immediately after the infusion there was a slight further distention of the wounds. No significant increase in the volume of the uninjured feet was observed (fig. 8). The other two experiments showed similar effects.

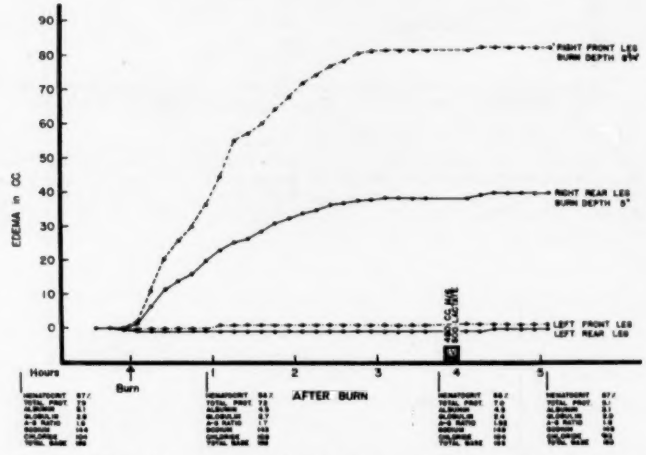


Fig. 8.—Effect of intravenous infusions on rate and degree of edema formation following a burn at 90 C. for fifteen seconds in dog B122. Infusion of 400 cc. of isotonic sodium lactate was begun four hours after injury. There was slight further increase in edema of the burned feet but no significant change in the volumes of the uninjured feet.

The hematocrit value, serum total protein, albumin-globulin ratio, sodium content, chloride content and total base were measured before and after injury and before and after the infusion. The changes observed were consistent with hemoconcentration following the burn and hemodilution following infusion (figs. 7 and 8).

COMMENT

It is true that the application of cold to a burn wound diminishes the rate of edema formation and therefore the rate of loss of plasma volume and that it may even diminish slightly the volume of edema

which has already formed before its application, but it is not necessarily true that cold is a treatment of choice for the burned patient.

Cold retards the loss of plasma volume but does not eliminate it. The wound volume slowly increases while the chilling continues, and though the volume reached may be less than that expected had the wound not been chilled, our experiments do not indicate a sparing of plasma volume adequate to indicate the use of cold on this basis. The sparing of plasma loss is also not a problem in a patient with a circumscribed burn but is most needed in the extensively burned patient. If sufficient cold is applied for a therapeutic effect to an extensive burn of the body surface, it will cause a drop in body temperature. Experiments using cold not cited in the observations of this paper were carried out on dogs with all four legs of each burned; there was such a drop in body temperature that survival was threatened.

It is reasonable to conclude that cold may retard the development of infection and diminish damage due to an impaired circulation, but cold also reduces the rate of the healing processes. Tempting though it may be to use cold in the therapy of burns, it must be recognized that an excessive use of cold, with either too severe a cooling application or too long an exposure, may in itself result in tissue damage. Until more is known of the critical temperature and period of exposure which can be employed with safety, it is considered wise to limit the use of cold to the temporary alleviation of the pain of burns of small extent. In this act it may be extremely useful.

SUMMARY

The effect of a cold water bath on the abnormal circulation of blood and lymph and on the rate of edema formation induced by a thermal burn was studied. The temperature selected for the cold bath was 10 C., inasmuch as this degree of cooling in itself has been shown to cause no damaging effect on tissues.

Exposure to cold alters the pattern of lymph flow and protein concentration. Lymph flow from a burned foot is sharply reduced during the entire period of immersion in the cold bath, regardless of whether cold is applied immediately after the burn or at some interval later. The rise in protein concentration of lymph and in rate of edema formation is also retarded. These changes occur apparently as a result of shunting of blood flow away from the damaged capillaries. On withdrawal of the foot from the cold, the rate of lymph flow and edema formation is accelerated and the rise in protein concentration of lymph resumed until it reaches or even exceeds the levels of the untreated foot.

Cold does not alter the pattern of arterial blood flow in the burned foot until removal of the foot from the cold bath is effected. This is in contrast to the pattern of lymph flow, which is strikingly altered only during the period of immersion in the cold. When exposure to cold ceases, there is an immediate rise in blood flow in the treated foot but no striking or consistent change in the untreated foot. This difference in flow pattern in the two feet indicates that the rise in blood flow in the treated foot is the result of a reflex locally governed.

Neither the intensity of the burn nor the duration of immersion in the cold bath altered the pattern of response in the lymphatic or arterial circulation. No consistent changes in blood pressure were established during infliction of the thermal injury, in the period immediately following injury or during therapy with cold.

The limitations of the use of cold in the therapy of burns are analyzed and discussed.

CIRCULATION OF THE BLOOD AND LYMPH IN FROSTBITE AND INFLUENCE OF THERAPEUTIC COLD AND WARMTH

An Experimental Study

LEON ROSENFELD, M.D.
JOHN L. LANGOHR, M.D.
CORA R. OWEN, Ph.D.
AND
OLIVER COPE, M.D.
BOSTON

FROSTBITE is a common injury of man transposed from temperate to cold climate, yet little is known of the physiologic disturbances it creates, and the treatment of it is still in the realm of empiricism. The adverse effects of this injury assumed special importance during the recent war, when these studies were undertaken.

The resemblance of frostbite to burns, the experimental observations of Lewis [1] and the experience in the early years of World War II in the treatment of immersion foot with cold [2] suggested that the disorder of the arterial and lymphatic circulation induced by frostbite might well be similar to that following burns. Accordingly, as a beginning to a better physiologic understanding and more rational therapy, the experimental studies of the circulatory disturbances of trauma due to burns were extended to frostbite, including the possible use of cold and warmth in treatment.

This work was aided by a grant from the Ciba Pharmaceutical Products, Inc., Summit, N. J.

From the Surgical Research Laboratories of the Harvard Medical School at the Massachusetts General Hospital.

The work described in this paper was done under a contract, recommended by the Committee on Medical Research, between the Office of Scientific Research and Development and Harvard University.

1. Lewis, T.: Observations on Some Normal and Injurious Effects of Cold Upon the Skin and Underlying Tissues: I. Reactions to Cold, and Injury of Normal Skin, Brit. M. J. **2**:795, 1941; II. Chilblains and Allied Conditions, ibid. **2**:837, 1941; III. Frostbite, ibid. **2**:869, 1941.

2. Webster, D. R.; Woolhouse, F. M., and Johnston, J. L.: Immersion Foot, J. Bone & Joint Surg. **24**:785, 1942. White, J. C., and Scoville, W. B.: Trench Foot and Immersion Foot, New England J. Med. **232**:415, 1945.

METHODS

Frostbite was produced experimentally by immersing the dog's foot in a liquid mixture of ethyl alcohol and solid carbon dioxide. Different degrees of tissue injury were produced by varying the temperature of the cooling mixture and the duration of the immersion. The desired temperatures of the immersion bath were obtained by changing the proportion of the two components with constant stirring.

The animal was anesthetized and prepared in a manner similar to that used in the studies of experimental thermal burns treated with cold (see previous paper). Under aseptic precautions the lymphatic trunks of both hindlegs were cannulated above the ankle; the circulating blood was heparinized.[3] The anterior tibial arteries were cannulated and attached to calibrated flowmeters and blood pressure manometers. A carotid artery was cannulated and the pressure within it recorded. After a period of stable blood flow had been assured, the hindfeet were immersed in the freezing mixture and the changes in the arterial and lymphatic circulations observed.

OBSERVATIONS

The circulatory pattern of frostbite of varying severity in the foot of the dog has been defined and the effect of both cold and warmth on it determined in twenty-seven experiments. In addition to the arterial and lymphatic flows, the edema formation, with its magnitude and composition, has been measured. The course of events in experiments involving frostbite of moderate severity is presented first, followed by the results of those illustrating minimal and severe frostbite. Experiments evaluating the effect of continued blood flow in mitigating the degree of frostbite and determining the use of varying temperatures as therapy are described in the subsequent sections.

CIRCULATORY PATTERN OF FROSTBITE

Moderate Frostbite.—With the dog under pentobarbital sodium anesthesia, the lymphatic vessels of both hindlegs cannulated, the blood heparinized, a flowmeter in each anterior tibial artery and the carotid blood pressure cannula recording, the effect of frostbite was examined. Before immersion in the freezing mixture a control hematocrit reading was taken at the time of heparinization. A period of stable blood flow was observed for one hour or longer. Control samples of lymph were obtained by gentle massage, there being no demonstrable spontaneous lymph flow in the resting uninjured extremity. The width of both feet was measured as a base line for judging edema formation. Frostbite of one foot was produced at a temperature of minus 18 C. for twenty minutes in one experiment and thirty minutes in another; the other foot in both experiments was kept as a control (chart 1).

On immersion in the freezing mixture, the foot blanches slowly over a period of two minutes, freezes gradually from the skin inward

3. The heparin (liquaemin®) was supplied through the generosity of Roche Organon, Inc., of Nutley, N. J.

and on removal is frozen solid. A flush rapidly appears three to four minutes after removal from the freezing mixture. Thawing of the frozen tissue starts both proximally and distally, the midportion being the last to thaw. Visible edema follows the thawing, and the foot assumes initially the shape of a dumbbell. The red color of the initial flush yields gradually to a cyanotic hue. Blebbing between the toes and

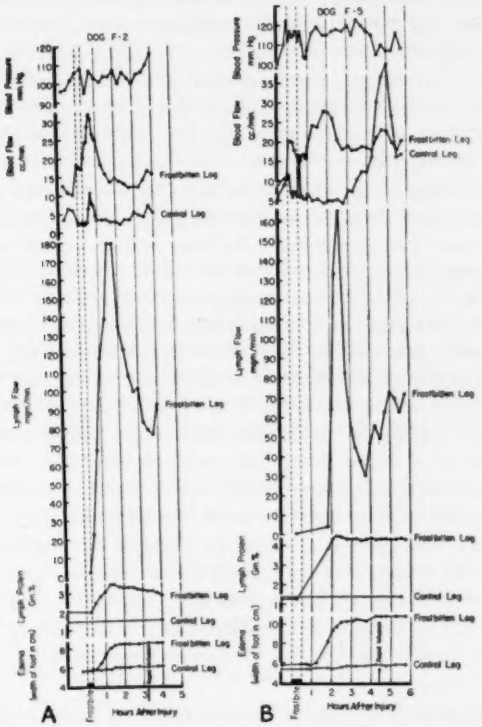


Chart 1.—*A*, effect of moderate frostbite on arterial and lymphatic circulation and on edema formation. *A*, frostbite was produced by immersion of one hindfoot in a bath of minus 18 C. for twenty minutes, the other foot being used as a control. *B*, frostbite was produced by immersion of one hindfoot in a bath of minus 18 C. for thirty minutes, the other foot being used as a control.

a generalized outpouring of exudate comparable to those following a burn appear. No changes were visible in the control foot.

The changes in arterial blood pressure were consistent only in the period immediately following withdrawal of the foot from the freezing mixture. While the foot was being immersed the response in blood pressure varied. In some of the experiments there was a slight rise

(chart 1 *B*); in others (not depicted) there was a slight fall or no change. During the period of immersion, however, there was usually no change although in some of the experiments there was a slow slight fall. On withdrawal of the foot there was an immediate decisive fall in pressure in all experiments. From this fall there was a gradual recovery to the level at the time of immersion, manifest in twenty to thirty minutes but usually not complete for an hour. Subsequent changes were dependent on the circulating volume, the effect of the reinfusions and anesthesia.

The mean arterial pressures recorded by the manometer connected with the flowmeters and the cannula in the carotid artery were essentially identical in all experiments; therefore, only the carotid pressure is depicted in the charts.

On immersion of the foot in the freezing mixture the blood flow rose in some experiments but did not change in others. Throughout the immersion there was a progressive decrease in flow. In the experiment with the twenty minute immersion this decline was slight (chart 1 *A*); in that with the thirty minute immersion it was greater (chart 1 *B*). The amount of decrease in flow was proportionate to the severity of the freezing. After removal, not immediately but with thawing, there was an increase in flow. No decrease in flow was noted with the fall in blood presure occurring immediately after withdrawal. When thawing was advanced, and at the time of the rise in blood pressure, there was a further increase in blood flow. The maximal blood flow was reached at the peak of the blood pressure rise in one experiment (chart 1 *A*) but not until twenty minutes after the peak in another (chart 1 *B*).

The blood flow in the control foot changed but little and inconsistently on the initiation of the trauma to the opposite foot. Throughout the period of immersion of the other foot, there was no change in flow. On withdrawal of the injured foot there was a prompt sharp rise in the rate of flow, which was usually transient as compared to that in the traumatized foot.

In the frostbitten foot there was invariably an increase in flow and protein concentration of the lymph comparable to that following a burn and indicating increased capillary filtration. The onset of the flow of abnormal lymph was delayed by the freezing, an acceleration occurring with the thawing. Thus in the experiment with but twenty minute immersion the onset of spontaneous flow occurred immediately after withdrawal and the rate of flow reached its maximum in one hour and ten minutes after withdrawal (chart 1 *A*); in the experiment with longer immersion, thirty minutes, spontaneous flow was not established until an hour after withdrawal, and the rate had not reached its maximum until nearly two hours after withdrawal (chart 1 *B*).

The rise in lymph flow lagged behind that of the blood flow and reached its peak at the time of maximum edema. The peak was short lived and was followed by a decline, nearly as rapid as the preceding rise. The initial decline, however, lasted but one hour, did not fall to zero and was followed by a fluctuating flow.

The protein concentration of the lymph from the frostbitten foot rose with the onset of spontaneous flow to levels comparable to those following burns. In the moderate frostbite the protein concentration rose from 2.0 to 3.6 Gm. per hundred cubic centimeters (chart 1 *A*) and in the more severe frostbite from 1.3 to 4.4 Gm. The pink tinge of hemolysis was evident in the lymph immediately after thawing; its occurrence was transient.

In the control foot there was no spontaneous lymph flow and either no change or a slight rise in protein concentration but no more than that expected as a result of the continued massage needed to secure the samples.

Edema followed on the heel of thawing; its formation was rapid in feet frostbitten to this degree. After immersion for twenty minutes, the foot thawed quickly; edema was apparent in thirty minutes, and its peak was reached seventy minutes after withdrawal from the cold bath (chart 1 *A*). In the experiment with the thirty minute immersion edema formation was not evident until one hour after withdrawal and did not reach its peak until two hours after withdrawal from the bath (chart 1 *B*).

Minimal Frostbite.—Under experimental conditions identical with those described in the first section, one foot of a dog was immersed for fifteen minutes in a freezing mixture at a temperature starting at minus 5 C. and falling to minus 8 C. Blanching of the immersed foot was visible, but the tissues were not rigid on withdrawal. After withdrawal a flush immediately appeared.

The blood pressure changes were comparable to those recorded in the dog with the moderate frostbite (see chart 2 *A* and chart 1). The blood flow in the traumatized foot in the present experiment (chart 2 *A*) increased during the immersion, in contrast to the fall in that with the more severe frostbite accompanied with a freezing of the tissues (charts 2 *A* and 1 *B*). There was no increase in flow after withdrawal. The changes in flow encountered in the control foot were like those of the frostbitten foot.

The changes encountered in the lymphatic circulation indicated minimal damage to the capillaries of the frostbitten foot. There was a slight spontaneous flow immediately after the immersion, but two hours later the sample of lymph had to be obtained by massage. There was, however, a sharp rise in protein concentration after the immersion.

which was not seen in the control leg and therefore signified alteration in capillary permeability. No evidence of hemolysis was apparent in the lymph. (The lymph in the control foot was obtained only by massage.)

There was slight progressive edema formation, but it was no greater in the immersed foot than in the control foot. The edema was adjudged

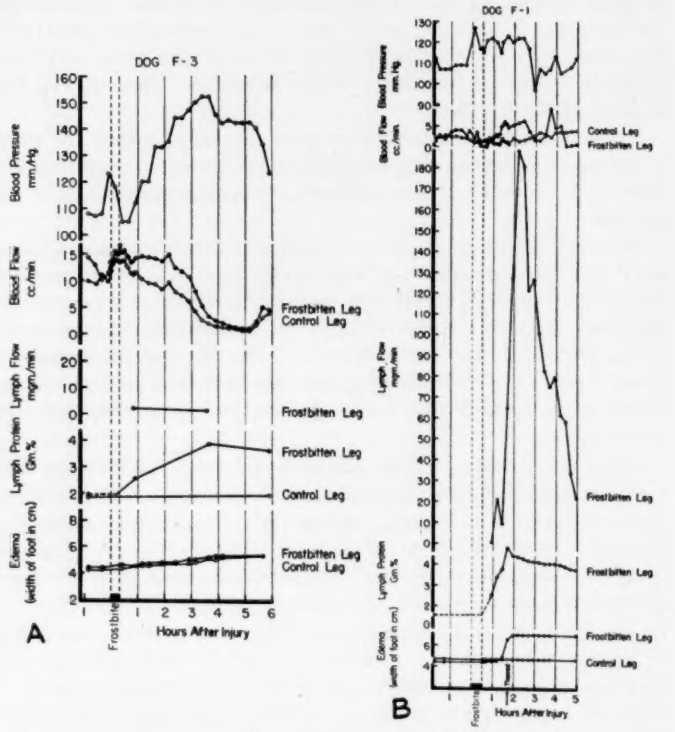


Chart 2.—*A*, effect of minimal frostbite on arterial and lymphatic circulation and on edema formation. Frostbite was produced by immersion of one hindfoot in a bath of minus 5 to minus 8 C. for fifteen minutes, the other foot being used as a control. *B*, effect of severe frostbite on arterial and lymphatic circulation and on edema formation. Frostbite was produced by immersion of one hindfoot in a bath of minus 25 C. for thirty minutes.

to be presumably the result of the dependency of the feet during the experiment.

The increase in protein concentration of the lymph and the length of the period of spontaneous lymph flow point to a damage as the result of the immersion in the cold bath. The absence of greater edema in the

immersed foot and the shortness of the period of spontaneous flow of lymph indicate that the damage from frostbite was minimal.

Severe Frostbite.—Immersion of the dog's foot in a freezing mixture at minus 25 C. for thirty minutes resulted in a severe frostbite (chart 2*B*). During immersion the foot froze rigidly, and it took one and three quarter hours to thaw completely. The blood pressure changes were comparable to those encountered in the previous experiments. The blood flow fell to zero during the period of immersion. With thawing, the increase in flow was slow, and thereafter the flow was irregular. The high peak of flow seen after the less severe frostbites was absent. In the lymphatic circulation there was a delay in the increase of flow and protein concentration during thawing. Evidence of hemolysis was present in the initial post-traumatic samples of lymph. The rate of edema formation was rapid after thawing. These changes in the lymph flow and protein concentration were comparable to those following a severe burn.

Effect of Interruption of Blood Flow on Degree of Frostbite.—Because of the decrease in blood flow encountered during immersion in cold and the cessation of flow with freezing, an attempt was made to evaluate the relationship of the reduction of blood flow introduced by the blood flow cannula to the degree of frostbite. The transitory ischemia occurring during cannulation had already been controlled in each experiment in the foot not frostbitten; no evidence of increased capillary permeability was observed.

During the period of immersion of both feet, the arterial circulation of one foot was interrupted by clamping the exposed anterior tibial artery. A frostbite of moderate degree was chosen—immersion for twenty-five minutes at a temperature starting at minus 18 C. and descending to minus 20 C. The changes in lymph flow and protein concentration and the increase in edema in the frostbitten, nonischemic foot were typical of those following the frostbite in the previous experiment (chart 3*A*). In the foot rendered ischemic during immersion there was evidence of greater damage. Freezing of the immersed tissues was grossly complete and the period of thawing prolonged. After the thawing, the greater rise in lymph flow and protein concentration and the more promptly appearing and increased volume of edema indicated greater damage during freezing. The greater damage in the ischemic foot is believed to be due more to the absence of the warming effect of circulating blood than to the anoxia of ischemia.

THERAPY IN FROSTBITE

The assay of the effect of cold on experimental frostbite was indicated not only because of a recommendation of its use in the therapy

of frostbite in the human being but also to test further the apparent similarity of the circulatory changes of thermal burn and frostbite.

Cold in the Therapy of Frostbite.—The effect of cold water therapy, at 10 C., on the abnormal arterial and lymphatic circulation and on the development of edema following frostbite was explored in three experiments. The findings in a typical experiment are shown in chart 3 *B*.

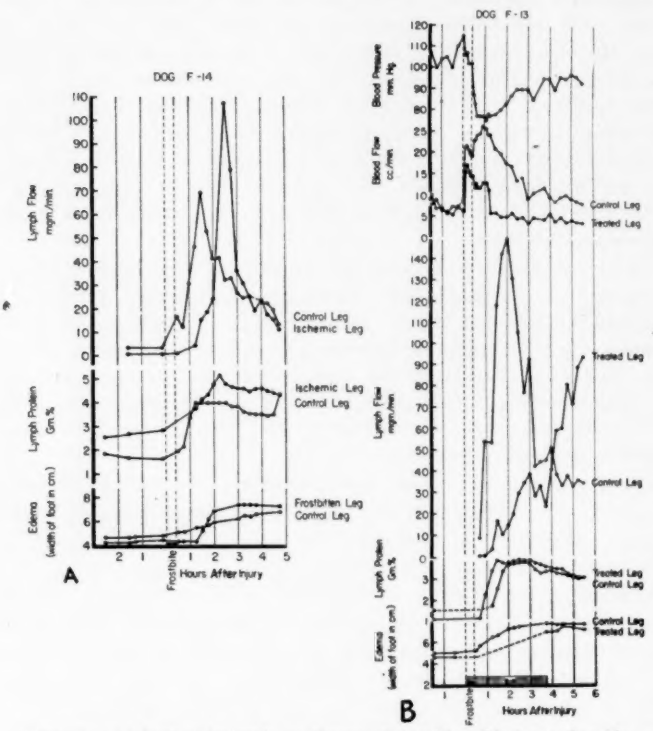


Chart 3.—*A*, effect of ischemia on degree of frostbite. Moderate frostbite was produced by immersion of both hindfeet in a bath of minus 18 to minus 20 C. for twenty-five minutes. During the period of immersion, the arterial circulation of one hindfoot was interrupted by clamping the exposed anterior tibial artery; the other foot was used as a control. *B*, effect of treatment with cold on the abnormal arterial and lymphatic circulation and the development of edema following frostbite. Moderate frostbite of both hindlfeet was produced by immersion in a bath of minus 18 to minus 20 C. for twenty-five minutes, and one of the frostbitten feet was then immersed in the treatment bath of 10 C. for three and three-quarter hours.

The reasons for the use of 10 C. are recounted in the previous paper ("The Effect of Therapeutic Cold on the Circulation of Blood and

Lymph in Thermal Burns"). The same experimental method was employed. The frostbite was that of moderate degree, a 25 minute immersion in a freezing mixture of minus 18 C. to minus 20 C. One of the two frostbitten feet was immersed in the bath of 10 C. immediately after freezing; the period of this therapeutic immersion varied from three and one-quarter to three and three-quarter hours. The frostbite produced the typical changes already described.

The blood flow to the treated and untreated feet was not significantly dissimilar. In the experiment charted, the blood flow to the treated foot was lower than that to the control foot even during the period of immersion.

The lymph flow from the treated foot was retarded throughout the period of treatment with cold. Immediately after its removal from the treatment bath, there was a sharp increase in flow, which reached a level higher than that from the control foot. The rise in concentration of lymph protein was also retarded, the final concentration reached being the same as that from the control foot.

The edema formation was also apparently slightly delayed by the treatment in the cold bath.

The delay in increase of lymphatic flow during immersion in the treatment bath and the prompt increase following removal from the bath indicate a local restraining mechanism comparable to that encountered in burns treated with cold.

Treatment of Frostbite with Warmth.—The therapeutic effect of a warm water bath, at 40 C., on frostbite was tried in five experiments. Before the inducement of frostbite, the effect of 40 C. was explored in one experiment. A ten minute immersion at this temperature produced a slight flush of the immersed foot but no change in the arterial inflow, lymph flow or protein concentration. The frostbite was produced by immersion at minus 18 C. for twenty-five minutes. After the frostbite one foot was immersed in the warm bath for periods varying from two and three-quarter to three and a half hours.

No significant differences were observed in the blood flow to the warmed foot as compared with that to the untreated foot. The lymph flow and protein concentration of the treated foot increased more promptly than those of the untreated foot. Consistent significant differences in the maximal protein concentrations of the lymph from the two feet were not noted. The concentration rose more slowly in the warmed feet. Evidence of hemolysis disappeared more rapidly from the lymph of the warmed feet.

The experience with these five experiments suggests that the differences in the behavior of the lymphatic circulation of the two feet are to be explained by the faster thawing of the foot placed in the warm bath.

COMMENT

We have examined experimentally the disorder of arterial and lymphatic circulation induced by frostbite. The abnormalities found are strikingly similar to those following a hot water burn. There is the same evidence of increased arterial blood flow, damaged capillary membranes and overloaded lymphatic trunks. The only major dissimilarity arises from the fixation of tissues when frozen; blood flow is reduced and even arrested if the freezing is deep. It is not until the tissues thaw that the circulatory pattern encountered after thermal trauma manifests itself.

The similarity of the circulatory disorder between frostbite and burns is seen in many of the details. The shunting of blood from the damaged capillaries as a result of treatment with cold water at 10 C. occurs after both types of injury. Blood flow, augmented by the injury, is not reduced by the treatment with cold, whereas both the lymph flow and the edema formation are restrained. That this apparent shunting of blood is controlled by a local reflex in both types of injury is suggested by the observation that the restraint of lymph flow and edema formation is not seen in the contralateral damaged but untreated foot.

Those who feel that edema is deleterious to a wound may be tempted to use cold in their therapy of frostbite. As in the treatment of burns, we are fearful lest prolonged exposure to even such a mild degree of cold as immersion in water at 10 C. would in itself lead to tissue injury.

Except for the acceleration of thawing which it induces, warmth used in treatment does not alter the pattern of circulatory disorder. There is no evidence that a shortening of the length of time the tissues stay frozen decreases or alters the nature of the injury to the cells. We therefore have obtained no evidence pointing to benefit from the use of warmth in the treatment of frostbite.

SUMMARY

Frostbite was produced experimentally by immersing the dog's foot in a liquid mixture of ethyl alcohol and solid carbon dioxide. Different degrees of tissue injury were obtained by varying the temperature of the cooling mixture and the duration of immersion. We have found that varying the degree of injury modifies the physiologic phenomena of frostbite but does not basically alter it.

The disordered arterial and lymphatic circulation induced by frostbite was examined. During the period of freezing, blood flow progressively decreases in proportion to the severity of injury; not until thawing begins does blood flow to the injured extremity increase. From the frostbitten foot there is invariably an increase in lymph flow and protein concentration comparable to that following a burn; the

onset of flow of abnormal lymph is delayed by freezing and greatly accelerated with thawing. The rise in lymph flow lags behind that of blood flow and reaches its peak at the time of maximum edema. The protein concentration of the lymph rises with the onset of spontaneous flow to levels comparable to those following a burn.

The effects of cold (10 C.) and warmth (40 C.) used as therapy on the abnormal arterial and lymphatic circulation of frostbite and the development of edema were investigated. No significant differences were found in the blood flow of the treated and untreated feet. In the therapy with cold, lymph flow from the treated foot as well as lymph protein concentration and edema formation is retarded. When warmth was used as treatment, the lymph flow and protein concentration of the treated foot increased more promptly than those of the untreated foot. Consistent significant differences in the maximal protein concentrations of the lymph from the two feet were not noted.

The significance of these observations is discussed.

EXPLORATIONS INTO THE PHYSIOLOGIC BASIS FOR THE THERAPEUTIC USE OF RESTRICTIVE BANDAGES IN THERMAL TRAUMA

An Experimental Study

FREDERIC W. RHINELANDER, M.D.
JOHN L. LANGOHR, M.D.
AND
OLIVER COPE, M.D.
BOSTON

ENTHUSIASTIC recommendations of the use of pressure dressings and plaster casts in the local treatment of burns have appeared from a number of clinics.[1] Pressure dressings are advised because they tend to limit swelling of the wound, while plaster casts, if applied immediately after injury, prevent swelling.[1c] Although nearly all authors agree that such restrictive dressings are beneficial to wound healing, they have been advocated for a variety of reasons. Allen and Koch [1a] hold that an occlusive pressure dressing restores the tissue pressure normally dependent on an intact integument and thus aids in the return of venous blood. They cited Blair [2] as pointing out that pressure

---

This work was aided by a grant from the Ciba Pharmaceutical Products, Inc., Summit, N. J.

From the Surgical Research Laboratories of the Harvard Medical School at the Massachusetts General Hospital.

The work described in this paper was done under a contract, recommended by the Committee on Medical Research, between the Office of Scientific Research and Development and Harvard University.

1. (*a*) Allen, H. S., and Koch, S. L.: The Treatment of Patients with Severe Burns, Surg., Gynec. & Obst. **74**:914, 1942. (*b*) Siler, V. E., and Reid, M. R.: Symposium on Burns: Clinical and Experimental Studies with the Koch Method of Treatment of Heat Burns, Ann. Surg. **115**:1106, 1942. (*c*) Glenn, W. W. L.; Gilbert, H. H., and Drinker, C. K.: The Treatment of Burns by the Closed Plaster Method, with Certain Physiological Considerations Implicit in the Success of this Technique, J. Clin. Investigation **22**:609, 1943. (*d*) Levenson, S., and Lund, C. C.: The Treatment of Burns of the Extremities with Close Fitting Plaster of Paris Casts, J. A. M. A. **123**:272 (Oct. 2) 1943. (*e*) Sellers, E. A., and Willard, J. W.: The Effect of Plaster Bandages and Local Cooling on Haemoconcentration and Mortality Rate in Burns, Canad. M. A. J. **49**:461, 1943. (*f*) Alrich, E. M., and Lehman, E. P.: Studies on Burns: I. Effect of Plaster Confinement Applied at Varying Intervals after Burning, Surgery **15**:899, 1944.

2. Blair, V. P.: The Influence of Mechanical Pressure on Wound Healing, Illinois M. J. **46**:249, 1924.

limits both venous and lymph stasis. Noticing that the dressings promote comfort and that the wounds showed minimal infection, Siler and Reid [1b] recommended pressure because it tends to prevent the loss of plasma from the circulation, a point on which Koch and others agree.

As far back as 1924 Blair used mechanical pressure on wounds because it limited "the amount of plastic material that pours into the wound," [2] a point which Drinker and his collaborators [1c] have emphasized recently in more finite protein terms. They pointed out that not only does plasma pour out of the circulation through the dilated and permeable capillaries into the wound but also that the proteins of the plasma eventually become coagulated in the interstices of the stretched wound. They stressed the fact that not only must these proteins eventually be redissolved during healing but that the coagulum may serve as a nidus for infection and lead to increased fibrosis and scarring. They also expressed the belief that stretching by edema tears the tissues and leads to scarring.

All these reasons, if proved, should be important in burn therapy. But after the clinical use of pressure dressings at this hospital [3] and a critical survey of the literature, three reservations seemed indicated. The first was a practical point: Is there a true sparing action on loss of plasma or is the edema fluid merely displaced; how far can pressure be counted on to limit loss of plasma in the extensively burned patient? It was noted that in patients with burns of the extremities, the pressure of elastic bandages, even though applied well above the burn, often failed to check the appearance of edema in the unburned, unbandaged tissues. If both hands and wrists and the face were burned, for example (areas ideal for pressure bandaging), edema appeared in the upper part of the arms, at the base of the neck and over the chest.

Our failure to restrain the loss of plasma by pressure could have been due to an inadequate application of it, a fault which might be corrected by using the plaster dressing as recommended by Drinker. On the other hand, since the edema collected in the unburned tissues, proximal to the burn on the arms and over the upper part of the chest, perhaps it became disseminated because the lymphatic trunks draining the wound were overloaded, a factor which a plaster dressing might improve but not altogether correct. It should also be pointed out that Siler and Reid hesitated to draw a definite conclusion from their experiments aimed at testing the efficacy of pressure dressings in sparing loss of plasma.

---

3. Cope, O., and Rhinelander, F. W.: Symposium on the Management of the Cocoanut Grove Burns at the Massachusetts General Hospital: The Problem of Burn Shock Complicated by Pulmonary Damage, Ann. Surg. **117**:915, 1943.

The second reservation had regard to the rationale: Is the local collection of edema so deleterious to wound healing? It has been repeatedly observed at this hospital that the swelling of a burn wound may disappear almost as rapidly as it came and that fibrosis, or scarring, is by no means a constant sequel of preexisting edema. Bleb fluid from a partial thickness burn often fails to coagulate, and whether it does or not, it is resorbed in less than twelve days if the roof of the bleb is intact (and the wound uninfected). These findings would not suggest widespread coagulation of protein in the wound spaces in the absence of infection. They would also not suggest that distention of itself tears tissue.

The presence of infection, of course, might increase the coagulation in situ of the proteins which have exuded from the blood; but is coagulation so deleterious? Glenn, Gilbert and Drinker [1e] offered experiments which they believed point to such unfavorable action. They compare the healing of the two feet of dogs burned equally. One foot of each dog was encased immediately after the injury in either a plaster mold or a light plaster bandage. The control foot was left uncovered. Healing proceeded much more rapidly, with less destruction of tissue and less final scarring, in the foot encased with plaster. The improved healing is unquestioned, but in the appraisal of the result they laid such emphasis on the absence of coagulated protein in the wound that they neglected to consider the mechanical protection offered by the plaster. The cast must have cut down, if not cut out, the repeated bacterial contamination which the uncovered foot received from the skin elsewhere, the tongue and the cage.[4] If the dog used the foot, the cast should have distributed the pressure and protected the foot from the trauma of licking.

The third reservation is the possible harm which might accrue from improper application of a pressure or plaster bandage, a warning stressed by Glenn, Gilbert and Drinker.[1e] If the bandage does not include the most distal portion of an extremity, even though unburned, gangrene may result. Because of the haste which may necessarily accompany care of disaster casualties and the length of time needed to apply an effective restrictive dressing, particularly plaster, the virtues of such a dressing must outweigh this danger before such therapy can be recommended.

We agree with Levenson and Lund [1d] that the reports on the clinical use of plaster bandages, and particularly those of Glenn, Gilbert and

4. The skin of dogs is heavily contaminated with fecal organisms, including the clostridia (Pope, A.; Zamecnik, P. C.; Aub, J. C.; Brues, A. M.; Dubos, R. J.; Nathanson, I. T., and Nutt, A. L.: The Toxic Factors in Experimental Traumatic Shock: VI. The Toxic Influence of the Bacterial Flora, Particularly Clostridium Welchii, in Exudates of Ischemic Muscle, J. Clin. Investigation **24**:856, 1945. Langohr, J. L.; Owen, C. R., and Cope, O.: Unpublished data).

Drinker [1c] on dogs, were so interesting that a more extended survey of their usefulness should be made. Since some of the supposed advantages and our own reservations are not susceptible to controlled testing on chance burns in the human being, resort was made to experiments on dogs, following the lead of Glenn, Gilbert and Drinker. Attention has been focused on the arterial and lymphatic circulation and their influence on the state of the wound. The observations bear only indirectly on the nutrition of the wound, for direct methods of sufficient accuracy have not been developed to compare the oxygen tension, for example, of the wound treated with a cast with that of the untreated wound.

EXPERIMENTS

The experimental animals were dogs of 18 to 20 Kg. They were anesthetized with pentobarbital sodium intravenously except in 2 cases in which sodium barbital was employed. The hair of the hindlegs was clipped closely. The method of burning was to plunge both hindfeet, to just below the ankle joint, for fifteen seconds into hot water at either 100 or 90 C. Immediately after burning, a thin skin-tight plaster bandage was applied to one foot, evenly without pressure, extending about 2 inches (5 cm.) above the burned area. The other foot was not enclosed in a cast and in the last experiments was covered with a dressing of loose petrolatum gauze. The surgical procedures, described under the separate headings, were performed with aseptic precautions, and the operative wounds were closed as much as the cannulas permitted. The collection of lymph samples from the cannula was not carried out aseptically, and the citrate solution used in the blood pressure determinations was not sterile.

In all, 33 dogs were used. In some experiments one type of observation was made, but in most data on various aspects were obtained.

1. *Lymph Flow.*—In experiments on 10 dogs the lymphatic vessels of the hindfeet just above the ankle were cannulated in routine manner. Lymph was collected for analysis over periods before burn and after burn. After the feet had been burned, one foot was enclosed in a cast and the other was not.

The results are shown in table 1. The initial increase in rate of lymph flow after the burn was more rapid in the foot with a cast. The rate rose, however, to a higher level in the foot without a cast, which confirmed the findings of Drinker [1c] with burns at 100 C. The same was true whether the burn was at 90 C. or at 100 C. and whether the feet were dependent or horizontal after the burn. The findings were consistent with one exception.

With the feet dependent, the 100 C. burn tended to produce a faster subsequent decrease of lymph flow in the foot with a cast (two of three

experiments), as Drinker [1c] observed with burns at this temperature. The 90 C. burn, on the other hand, led to a more rapid decrease in the foot without a cast (three of four experiments). With the feet horizontal and the burn at 90 C. (three experiments), the rate of subsequent fall of lymph flow averaged the same. Over the whole series of experiments there was thus no constant difference between the feet with a cast and those without a cast as far as the rate of subsequent fall of lymph production, after the initial rise following the burn, was concerned.

The effect of an intravenous infusion of isotonic sodium chloride solution was studied in 5 dogs. There was an almost immediate effect of increasing lymph flow. No difference was observed between legs treated with a cast and untreated legs as regards the amount and the rapidity of increased flow.

TABLE 1.—*Relative Rate of Lymph Flow From Feet With and Without Casts After Burning for Fifteen Seconds*

		Period of Increasing Flow						Subsequent Period of Decreasing Flow, Sharper Fall		
		Sharper Rise			Higher Peak Reached					
	No. of Dogs	Foot With Cast	Foot Without Cast	Same, Both Feet	Foot With Cast	Foot Without Cast	Same, Both Feet	Foot With Cast	Foot Without Cast	Same, Both Feet
Burn at 100 C.; dogs on back; legs dependent....	3	3	..	..	..	3	..	2	..	1
Burn at 90 C.; dogs on abdomen; legs dependent	4	4	..	..	..	4	..	..	3	1
Burn at 90 C.; dogs on abdomen; legs horizontal.	3	2	..	1	..	3	..	1	1	1

2. *Lymph Protein Concentration.*—In the 4 dogs burned at 100 C. and in 5 of the 6 dogs burned at 90 C. in which the lymph protein concentration was measured it was consistently slightly higher in the foot with a cast than in the foot without one for the period of the experiment following the burn (chart 1). In the sixth dog burned at 90 C. the protein concentration was lower in the foot with a cast after the first forty-five minutes following the burn. In this animal the peak of lymph flow reached in the other foot was only slightly above that in the foot with a cast, less so than in the other experiments; lymph flow ceased in the sixth hour. It is believed that the cannulation of lymphatic ducts was a poor mechanical preparation, and the data on lymph are therefore to be discounted. In keeping with the difference in protein concentration of the two lymphs, there was observed a difference in chloride concentration; it was lower in the lymph with the higher protein concentration. These observations cover a period up to eleven and a half hours after burn.

The effect of an intravenous infusion of isotonic sodium chloride solution on lymph protein concentration was studied in 4 of the animals (chart 1). The protein concentration was diminished in all burned feet except one not treated with a cast. In three of the experiments the fall in concentration was greater in the feet enclosed in a cast and in two of these the concentration in the feet so treated fell below that in

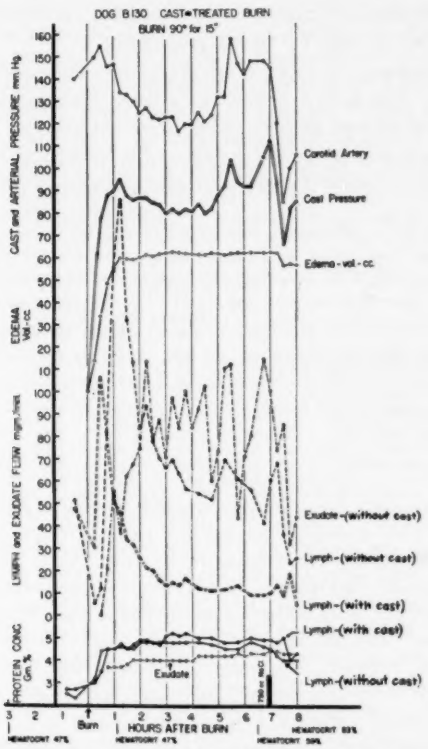


Chart 1.—Effect of restrictive plaster bandage on the lymph and exudate flow and protein concentration, edema formation and tissue and arterial pressure following burn of a hindfoot of a dog at 90 C. for fifteen seconds.

the feet without a cast. The maximal drop was noted at one to one and a half hours after the sodium chloride solution had been given.

3. *Venous Pressure.*—Venous pressures were compared after a burn of the hindfeet for fifteen seconds at 100 C. Determination of the venous pressure was carried out by inserting a large bore needle directly

into the main vein on the lateral aspect of the ankle. The needle was connected with a bromoform manometer, care being taken to eliminate the effect of gravity. Three of the experiments were considered satisfactory technically. In two of them the venous pressure showed a slight drop after the burn, but there was no significant difference between the legs with a cast and those without a cast. In 1 animal there was a slight rise after the burn and then a drop in both legs. The pressure in the leg without a cast stayed somewhat higher, the difference in height ranging between 0.5 and 1.0 cm. of bromoform.

4. *Arteriovenous Oxygen Differences.*—Preliminary experiments indicated that after a burn there was a large discrepancy between the venous oxygen content of blood taken from the femoral vein and that of blood from a vein in the lower part of the leg just above the burned area. The arteriovenous oxygen difference became extremely low when

TABLE 2.—*Arteriovenous Oxygen Differences (Values in Volumes Per Cent) in Blood Taken from the Femoral Artery and the Ankle Vein*

Dog No.		Before Burn	After Burn			
			1 Hour	3 Hours	6 Hours	10 Hours
B94	Foot with cast	0.8	0.0	0.1	1.5	0.5
	Foot without cast	0.0	0.0	0.1	0.2	1.2
	Control forefoot	2.2	0.4	0.3	2.6	2.4
B96	Foot with cast	3.6	0.0	0.1	0.2	1.1
	Foot without cast	3.8	0.2	0.1	0.2	1.1
	Control forefoot	3.6	0.9	0.8	0.9	2.7
B98	Foot with cast	2.9	1.3	2.1	1.5	2.8
	Foot without cast	2.8	0.6	0.8	0.9	2.7
	Control forefoot	1.0	0.9	...	1.2	2.7

the venous blood was taken from just above the site of the burn. Seven experiments were therefore carried out using a burn of 100 C. for fifteen seconds, venous blood being taken at the ankle and the arterial blood at the groin. In three the arteriovenous oxygen difference reached the lowest level in the leg without a cast, while in four it reached it in the leg with a cast. The difference between the values for the two legs was not significant, however, as is shown in table 2, which summarizes the data of the last three experiments performed in this series.

5. *Blood Flow.*—Measurement of the rate of blood flow through the arteries of the burned hindfeet, one in a cast and the other not, was made by means of flowmeters. The dogs were heparinized. The burns were for fifteen seconds at 90 C.

The flowmeters were of the constriction type with two verticle side arms, one proximal and one distal to the constriction, connected with each other by a U tube.[5] As the blood flowed through the con-

5. Drs. Gordon K. Moe and Dr. Friedrich W. Klemperer aided us in the construction and use of the flowmeters.

striction, the differential in height of the blood columns in the proximal and distal limbs of the U tube gave a measure of the pressure gradient on the two sides of the constriction. The flowmeters, which were made of glass tubing, were calibrated by running through them the dog's heparinized blood at known rates of flow. A table for each flowmeter was constructed from which the experimentally observed rates of flow were extrapolated. The primary aim of the experiment was to compare the changes in flow in the legs with a cast and those without a cast rather than to measure absolute flow in either. In application, the artery under observation was divided. Each end of the flowmeter was connected by a short piece of rubber tubing to a glass cannula inserted in the proximal and distal limbs of the artery. The top air-containing portions of the U tube of the flowmeter were connected by a Y tube to a mercury manometer in order to give a record of the blood pressure in the same artery in which flow was being recorded. Further details of the flowmeter method, including an illustration, are given in a subsequent paper.

In the first four experiments simultaneous recordings from the two femoral arteries were made. Each foot below the ankle was burned and a cast applied to one foot. An immediate rise occurred in the flow in each leg and then a gradual fall for the eight hours of the experiment. When a composite graph was made of the flows from the two legs in each of these four experiments, no significant differences between them were observed.

In order to evaluate more closely the blood flow through the burned portion of the legs alone, flowmeters were inserted into each anterior tibial artery, just above the ankle, in 3 animals. After the flowmeter had been inserted, the other main artery to the foot was ligated. In two experiments the flow for the first eight hours after burn was observed. In 1 case the flow in the two legs rose rapidly to essentially the same height and then showed the same subsequent slow fall. The maximum flow for the two legs was 45 to 50 cc. per minute at ten minutes after burn whereas the preburn rate had been 10 to 15 cc. per minute. In the other case the flows started at similar preburn levels. The first post-burn readings, made at one half hour, showed that the flow in the leg with a cast was at its maximum of 33 cc. per minute. The flow in the leg without a cast did not reach its maximum, a slightly less high level, until three hours later.

In the third dog with flowmeters in the anterior tibial arteries, the rate of flow for the second eight hours after burn was studied. The dog was burned, and the cast was applied immediately to one leg and loose petrolatum gauze to the other. The animal was kept under light anesthesia with pentobarbital sodium given intraperitoneally during the

first eight hours after burning, and the flowmeters were then inserted.[6] No significant differences were observed between the leg with a cast and the other leg. The flow in each leg continued to fall off during the period of observation from an average of 15 to 25 cc. per minute down to an average of 4 to 8 cc. per minute at sixteen hours after the burn.

6. *Tissue Pressure Beneath the Cast.*—The pressure which existed between the surface of a foot which had been burned and the inside wall of a cast surrounding this foot was measured by inserting a thin-walled rubber bulb under the cast at the time the latter was applied immediately after the burn. The rubber bulb was filled with water and connected with a mercury manometer which recorded on a smoked drum. An adjustable pressure bottle was attached to the recording system in such a manner that the volume of fluid within the rubber bulb under the cast could be kept constant at all times when a pressure reading was being recorded. Adjustment of the fluid volume within the rubber bulb was made at frequent intervals, and a tracing of the cast pressure was recorded simultaneously with a tracing of the carotid blood pressure on the same drum (chart 1).

The cast pressure was recorded in seven of the experiments in which the hindfeet were burned for fifteen seconds at 90 C. and in which the lymphatic vessels of the ankle had been cannulated. The end pressure in the lymphatic vessels themselves was not recorded. The lymph was allowed to flow freely. The lymph flow and the lymph protein concentration have been recorded in the previous sections. In six of the experiments the mean carotid arterial blood pressure was recorded simultaneously.

The cast pressure rose rapidly after the burn (chart 1). It reached its maximum in one to one and one-half hours. After having reached the maximum it varied closely with the blood pressure and in the various experiments ranged from approximately one half to two thirds of the mean arterial pressure.

Various factors influenced the relationship between cast pressure and blood pressure. In order to demonstrate these, two graphs were constructed for each of the 6 animals in this series, one of which is reproduced (chart 2). In graph *A* (the lower of the two graphs) the difference between mean arterial blood pressure and cast pressure is plotted as ordinates against the time after burn as abscissas. As the cast pressure approached its constant relationship with the blood pressure, the curve flattened out. High points on this curve, then represent

6. Up to the time of the insertion of the cannulas the dog had been placed on its side. In order to insert the flowmeters, the dog was placed on its back, the position used in the previous experiments. Respirations, however, faltered, and the animal became cyanotic. It was returned to its side, with slow improvement, and the operation and experiment were completed in this position.

greater than average difference between blood pressure and cast pressure, and low points represent less than average difference. Each point on the graph has been given a number corresponding with the numerical sequence of half-hour periods following the burn.

In graph *B* (the upper of the pair of graphs in chart 2), the mean arterial blood pressures at each half-hour reading are plotted as ordinates against the corresponding cast pressures as abscissas. This gives a series of points which are designated with the same numerals, corresponding to half-hour periods after

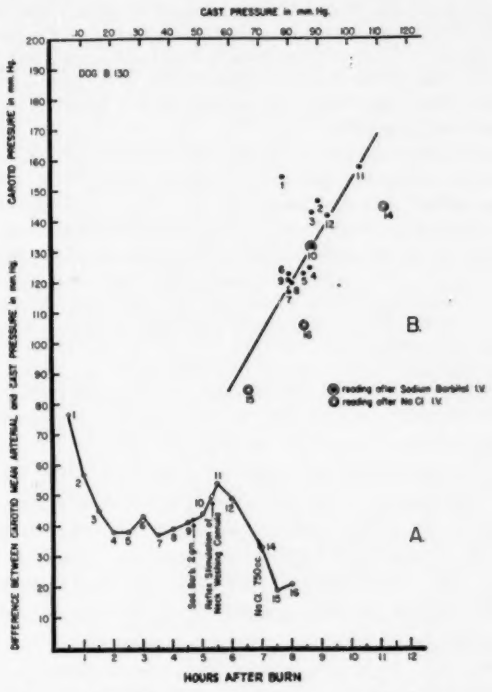

CAST PRESSURE in mm Hg.
CAROTID PRESSURE in mm Hg.
DOG B 130
B.
reading after Sodium Barbital I.V.
reading after No Cl I.V.
DIFFERENCE BETWEEN CAROTID MEAN ARTERIAL and CAST PRESSURE in mm Hg.
A.
HOURS AFTER BURN

Chart 2.—Relationship of cast pressure to arterial blood pressure.

burn, that are employed in graph *A*. Graph *B* for each animal indicates that at a higher systolic blood pressure there is normally a greater difference between cast pressure and blood pressure than there is at a lower blood pressure. This fact accounts for some of the points in graph *A* of the various experiments which were situated unusually high above the horizontal mean of the graph.

The type of graph designated as *B* serves to demonstrate variations from the normal range in the cast pressure versus blood pressure relationship when a large amount of isotonic sodium chloride solution was rapidly injected intravenously. That such an injection produced a narrowing of the cast pressure-

blood pressure difference had been suggested but not proved by graph *A*. The method of plotting employed in graph *B* eliminates the variable introduced by different levels of blood pressure and demonstrates that this narrowing was a true effect of the sodium chloride solution irrespective of changes in blood pressure. Thus in graph *B* for each animal the points following the intravenous injection of isotonic sodium chloride solution lie farthest to the right of and below the mean of all the points recorded.

Another extrinsic factor which might have altered the cast pressure–blood pressure relationship was the intravenous injection of pentobarbital sodium to supplement the anesthesia. Two successive doses of this drug within half an hour led to a relative increase in the cast pressure with respect to the blood pressure in one experiment. A single large dose produced the same effect in another. When smaller doses of supplementary barbiturates were administered to these 2 dogs, and to other dogs, there was no demonstrable effect on the cast pressure–blood pressure relationship.

All the abnormally low points on graph *A* for the 6 dogs are explained by the administration of either isotonic sodium chloride solution or a large dose of pentobarbital sodium. All the abnormally high points in graph *A* of the six experiments covering up to nine and a half hours after burn are accounted for by the normal lag in cast pressure which takes place when the blood pressure goes to high levels. For example, the high point 11 on graph *A* of dog B130 (chart 2) followed reflex elevation of the blood pressure from manipulation of the neck when the carotid cannula was washed after clotting. Graph *B* demonstrated that point 11 lay near the mean.

7. Edema in Legs Not Treated with a Cast.—In 5 of the dogs in which tissue pressure beneath the cast was studied, the swelling of the simultaneously burned opposite hindleg, not enclosed in a cast, was recorded in a plethysmograph. In four experiments the leg was suspended vertically, and in the fifth experiment it was held horizontally. Oil was used in the plethysmograph so that the exudate from the burned foot could be recovered and measured separately. The oil which was displaced as the foot swelled was collected in a buret from which was read in cubic centimeters the amount and rate of edema formation.

In all experiments a rapid increase in edema was observed for the first one and a quarter to two hours after the burn (chart 1). In three of the experiments with the legs dependent, the maximum level was reached within the first two hours, which was maintained until the infusion of isotonic sodium chloride solution (chart 1). In the fourth instance, after the maximum initial rise a further gradual rise continued until the end of the experiment. In the experiment with the legs horizontal, a gradual rise continued until three and a half hours after burn, when it leveled off.

The edema formation corresponded with the rise in cast pressure on the opposite foot, but with the expected lag. As would also be anticipated, the effects on edema of blood pressure variation and adminis-

tration of sodium chloride solution were much less than the corresponding effects on the cast pressure.

8. *Rate of Exudate Formation in Legs Not Treated with a Cast.*—The exudate collecting under the oil at the bottom of the plethysmograph in four of the experiments described in the previous section was drawn off periodically by means of a separatory funnel, and its volume was measured. The exact moment when exudate formation began could not be determined. The moment when the first drop of exudate was large enough to fall to the bottom of the plethysmograph varied in the four experiments from between three-quarters of an hour and one and one-half hours after burn. Drops of exudate appeared in all areas of the burned skin and not merely from between the toes where actual blebs formed. The maximum rate of exudate formation was observed in the plethysmograph at from one and three-quarters to two and one-quarter hours after burn in the 3 dogs whose legs were in the dependent position (chart 1). In the experiment with the leg horizontal, the maximum exudate formation occurred at three hours after burn. Variations in rate of exudate formation with changes in blood pressure were observed in all four experiments and were of the same order.

9. *Exudate Protein.*—The protein concentration of the exudate fluid in each sample was measured in the four experiments in which exudate was recovered. In all instances the amount of exudate protein was lower than the protein concentration of the lymph collected from the lymphatic trunk of the same leg (chart 1).

COMMENT

The experimental explorations into the disordered physiologic changes in the burn wound supported by a rigid plaster of paris dressing recorded in this paper do not provide the unequivocal evidence needed to guide us in the use of pressure dressings in the treatment of burns. Changes encountered immediately after the burn which are apparently in favor of pressure dressings are supplanted with the passage of time. The other factors believed to favor these dressings, such as the decrease in proteins coagulated in situ and localization of infection, are still experimentally unproved.

The most emphasized benefit to be derived from pressure dressings is the sparing of the loss of plasma into the burn wound. However, Siler and Reid,[1b] after their experimental investigation which tended to show such a sparing, wisely pointed out in the discussion that the data they obtained were probably within the experimental error of the method used. Of like negative value are our own findings. At first sight the observation that the lymph flow from a burn wound is reduced by a rigid plaster wall applied immediately after injury should indicate

a diminished loss of plasma. As the experiment is followed, however, it becomes clear that the increased flow after burning is not sufficiently reduced by the cast for the lymphatic vessels to be able to carry it. Unable to return to the blood stream all the fluid flowing through the damaged capillaries, the lymph piles up as edema in the interstitial spaces proximal to the cast. With the passage of time this edema may slowly reach the volume it would have been had the restricting dressing not been applied.[7] Though in the first hours the volume of plasma lost may be reduced, it appears that eventually it may be the same as in the wound not treated with a cast. More quantitative evidence is, however, needed on this point.

The observations that the arterial blood flow to a burn wound is not reduced and that the arteriovenous oxygen difference is not altered by the plaster dressing suggest that no harm accrues to the wound's circulation and nutritional environment from the restricting pressure. It is possible that the benefit which clinically appears to accrue from the use of the restrictive dressings comes from the immobilization of the wound provided by the dressing. Motion of the burn wound increases lymphatic flow and displaces edema proximally in the interstitial spaces. These both have the effect of lowering the tissue pressure in the wound, which permits augmented seepage out of the capillaries. Because of these effects of motion and because the loss of plasma is retarded, restrictive, immobilizing dressings are presumably indicated in the care of burn wounds. They must not be used, however, with the idea that the need for plasma therapy in burn shock will be materially reduced. And whether the benefit from their use outweighs the danger of gangrene from improper application, particularly that of the plaster dressing, will depend on the intelligence with which such dressings are used.

SUMMARY

The effect of a restrictive plaster bandage on the disordered physiologic changes in the burn wound has been explored experimentally in burned feet of dogs. Although the increased flow of lymph from the burn is reduced toward normal, it is not sufficiently reduced to permit

7. Our findings are not in agreement with the point of view of Glenn, Gilbert and Drinker [1c] that "the enclosure of the burned part in a plaster of Paris dressing prevents abnormal leakage from the injured capillaries." The volume of lymph flowing from a burn wound restricted by plaster is not as great as from a wound allowed to swell, but it is far greater than normal, indicating an increased leakage of plasma fluid into the wound through the damaged capillary membrane. The inflow of arterial blood does not meet a truly rigid wall as conceived of by Glenn and others; the continued outflow of venous blood and lymph provides elasticity. The pressure within the cast does not reach mean arterial pressure.

the lymphatic vessels to carry the load, and edema piles up in the interstitial spaces of the leg proximal to the plaster bandage.

Loss of plasma volume is thus retarded but not eliminated and presumably not reduced. The concentration of the protein in the lymph flowing from the bandaged foot is slightly higher than in that from the foot allowed to swell, which indicates a greater resorption of water into the venous blood.

Venous pressures, arteriovenous oxygen differences and arterial blood flow were not altered by the plaster bandage.

Tissue pressure, measured as the pressure between skin and plaster bandage, approached but never reached mean arterial blood pressure. Arterial blood therefore does not flow against a rigid wall, the outflow of venous blood and lymph providing some elasticity.

The protein concentration of exudate fluid seeping out onto the surface of the burned skin is slightly lower than that of the lymph flowing from the same wound. This indicates either that water is resorbed from lymph, lymph being more concentrated than extracellular tissue fluid, or that part of the protein of the tissue fluid is strained as the fluid seeps through the skin. If the latter were true, the concentration of protein in the bleb fluid of a burn in the human being might be lower than that of the subcutaneous edema fluid.

The possible benefits and limitations of restrictive dressings are discussed.

MORTALITY AND MORBIDITY IN SURGERY OF THE BILIARY TRACT

A Comparison of Two Consecutive Ten Year Periods

WILLIS G. DIFFENBAUGH, M.D.
Clinical Instructor in Surgery, University of Illinois College of Medicine
AND
SELIM W. McARTHUR, M.D.
Clinical Professor of Surgery, University of Illinois College of Medicine
CHICAGO

ADVANCEMENTS made in the last few years in preoperative and postoperative care, such as better intravenous administration of fluids, amino acid and protein hydrolysates, antibiotic drugs like penicillin and the sulfonamide compounds, more available blood transfusions, vitamin K and better anesthetic procedures, should all reflect on the mortality of surgery of the biliary tract. A report in 1946 by Sanders [1] suggested that the mortality rate had not been reduced appreciably, whereas Orr's [2] recently reported statistics showed a definite improvement (table 1).

In this series the mortality has been markedly decreased in the last ten years as compared with the preceding ten year period (table 2). The decrease was from 8.3 per cent in the years 1927 to 1937 to 2.8 per cent in the years 1937 to 1947. The improvement is noted particularly in the cases of acute cholecystitis and in the marked decrease in deaths due to infection and peritonitis. The lowered mortality in this group is of interest in view of the controversy regarding immediate surgical treatment of acute cholecystitis versus delayed treatment. In spite of the fact that in the last ten year period there was a greater delay from the time of hospitalization to the time of operation, there has been a sharp decline in the mortality (table 3). Perhaps the lowered mortality credited by some authors to earlier operation may be due to the use of the antibiotics and to improved preoperative and postoperative care.

From the Surgery I Service of St. Luke's Hospital.

Presented before the Chicago Surgical Society May 7, 1948.

1. Sanders, J. T.: Biliary Tract Surgery: An Inquiry into the Reason for the Thirty-Three Deaths in Four Hundred and Fifty-Three Operations, South. M. J. **39**:961 (Dec.) 1946.

2. Orr, T. G.: A Study of the Mortality Rate in a Series of Cholecystectomies, Am. J. Digest. Dis. **14**:89 (March) 1947.

The incidence of perforations of the gallbladder in this series was 18.1 per cent in the first ten year period, with a mortality of 33 per cent, and 26.6 per cent in the second ten years, with no deaths. Cowley and Harkins [3] in 1943 reported an incidence of perforation of

TABLE 1.—*Mortality in Surgery of the Biliary Tract*

Author	Year	Number of Cases	Mortality, %
Heuer [4]	1934	36,623	6.6
Eliason and Erb, Ann. Surg. **101**:460 (Jan.) 1935	1935	537	8.0
Heyd [5]	1940	557	7.7
Sanders [1]	1946	453	7.2
Orr [2]	1946	558	2.8
Diffenbaugh and McArthur	1927 to 1937	408	8.3
	1937 to 1947	417	2.9

TABLE 2.—*Mortality Statistics*

Condition for Which Operation Was Performed	Years	Cases	Deaths	%
Total mortality	1927 to 1937	408	34	8.3
	1937 to 1947	417	12	2.8
Acute cholecystitis	1927 to 1937	33	10	30.3
	1937 to 1947	30	1	3.3
Chronic cholecystitis with involvement of the common duct	1927 to 1937	85	16	18.8
	1937 to 1947	62	7	11.2
Chronic uncomplicated cholecystitis	1927 to 1937	270	4	1.4
	1937 to 1947	295	0	0.0
Malignant processes	1927 to 1937	9	3	33.3
	1937 to 1947	11	4	36.3
Secondary procedures on the common duct	1927 to 1937	11	1	9.0
	1937 to 1947	19	0	0.0

1927 to 1937 70.2% of the deaths were in patients over 50 years of age.
1937 to 1947 61.5% of the deaths were in patients over 50 years of age.

TABLE 3.—*Acute Cholecystitis*

	1927 to 1937	1937 to 1947
Total cases	33	30
Males	31%	45.1%
Females	69%	54.9%
Perforations	18.1%	26.6%
Average time from onset of symptoms to hospitalization, days	3.2	2.2
Delay from time of hospitalization to operation, days	3.9	6.6
Complications involving the common duct	15.1%	6.6%
Stones	78.7%	90.3%
Mortality *	30.3%	3.3%

* Eighty-one and one-tenth per cent of the deaths were due to peritonitis or infection.

13 per cent in 2,261 cases of acute cholecystitis, with a mortality of 20.8 per cent in the cases of perforation, and Heuer [4] in 1934 reported an incidence of 20 per cent, with a mortality of 45 per cent.

3. Cowley, L. L., and Harkins, H. N.: Perforations of the Gall Bladder, Surg., Gynec. & Obst. **77**:661 (Dec.) 1943.

4. Heuer, G.: Factors Leading to Death in Operations upon the Gall Bladder and Bile Ducts, Ann. Surg. **99**:881 (June) 1934.

The mortality in cases involving the common duct decreased from 18.8 to 11.2 per cent. There is an inevitable increase in mortality in these cases, approximately three times that for cases of uncomplicated chronic cholecystitis. The common duct was explored in 25.9 per cent of cases in the 1927-1937 series and in 17.3 per cent of cases in the 1937-1947 series and stones were found in 28.2 and 36.6 per cent respectively (table 4). It is noted that in approximately one fourth of the cases in which the common duct was explored there was no jaundice or history of jaundice, yet stones were found in a considerable percentage (15.8 and 35.2 per cent). In the cases in which there was exploration of the common duct without drainage it was carried out through the stump of the cystic duct. The cystic duct was then ligated. In all cases in which the common duct was incised for exploration drainage was instituted. T tubes were used more frequently in the last ten years than in the preceding ten. Before good solutions were available for intravenous administration a small catheter was frequently passed through the ampulla into the duodenum for the instillation of fluids and bile and a catheter passed up the duct for drainage. This method was used frequently in the first ten year period.

TABLE 4.—*Complications Involving the Common Duct*

	1927 to 1937	1937 to 1947
Primary exploration of the common duct	25.9%	17.3%
Stones	28.2%	36.6%
Jaundice	77.6%	71.8%
Stones	31.8%	38%
No jaundice or history of jaundice	22.3%	23.9%
Stones	15.8%	35.2%
Drainage of the common duct	83.5%	74.6%
T tubes	2 cases	34 cases
McArthur double catheter	48 cases	15 cases
Single catheter	21 cases	4 cases
Secondary exploration of the common duct	11 cases	19 cases
Jaundice	62.5%	83.3%
Stones	54.5%	57.8%

The mortality for secondary procedures on the common duct was 9 per cent in the first ten year period; in the last ten years there were no deaths. Heyd [5] has stated that whereas the mortality in cases involving the common duct is about 11.3 per cent when the exploration is performed at the time of the original cholecystectomy, in secondary choledochotomy the mortality is 350 per cent greater, i. e., the rate is 38.6 per cent.

Table 5 lists both minor and fatal complications occurring in this series. Pulmonary, vascular and hepatic complications were as frequent

5. Heyd, C. G.: Factors in the Mortality in 4,000 Operations upon the External Biliary System, Ann. Surg. **111**:820 (May) 1940.

in the last ten years as in the first ten, but less fatalities resulted. Hemorrhage and infection as complications were markedly decreased in the last ten years as compared to the previous ten year period Chart 1 shows this graphically.

The causes of death in this series were obtained from clinical records and from the findings at postmortem examination (1927 to 1937, autopsy in 53 per cent of cases; 1937 to 1947, autopsy in 75 per cent). Tables 6, 7 and 8 list the causes of death in the cases of acute cholecystitis, chronic cholecystitis and involvement of the common duct.

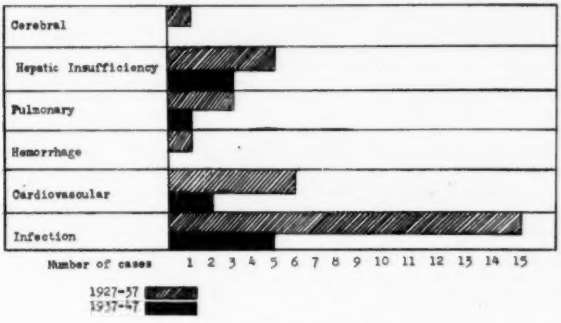


Fig. 1.—Causes of death.

TABLE 5.—*Statistics on Morbidity and Mortality*

	1927 to 1937	1937 to 1947
Pulmonary complications	7	10
Pneumonia	4	2
Pleurisy	1	3
Atelectasis	..	5
Cardiovascular complications	8	6
Coronary occlusion	2	1
Congestive failure	4	3
Pulmonary embolus	2	2
Hepatic insufficiency	2	6
Cholemia	2	1
Hepatorenal syndrome	..	5
Hemorrhage	8	1
Evisceration	..	1
Infection	29	9
Wound infection	17	3
Subdiaphragmatic abscess	..	1
Thrombophlebitis	..	2
Cholangitis	7	2
Peritonitis	5	1
Bile collections	1	1
Acute pancreatitis	..	3
Functional		
Postoperative colic	6	5
Distention	5	3

TABLE 6.—*Causes of Death in Cases of Acute Cholecystitis*

1927 to 1937		1937 to 1947	
Peritonitis	5	Pneumonia	1
Sepsis	3		
Pneumonia	1		1
Acute suppurative cholangitis	1		
	10		

TABLE 7.—*Causes of Death in Cases of Chronic Cholecystitis*

1927 to 1937		1937 to 1947
Peritonitis	2	No deaths
Coronary occlusion	1	
Hepatic necrosis	1	
	4	

TABLE 8.—*Causes of Death in Cases Involving the Common Duct*

1927 to 1937		1937 to 1947	
Peritonitis	5	Peritonitis	1
Suppurative cholangitis	1	Acute pancreatitis	3
Sepsis	2	Hepatorenal syndrome	1
Bronchopneumonia	2	Coronary occlusion	1
Pulmonary embolism	1	Pulmonary embolism	1
Cerebral embolism	1		7
Cardiac failure	2		
Coronary thrombosis	2		
Hemorrhage	1		
Cholemia	3		
	20		

TABLE 9.—*Causes of Death in Operations on the Gallbladder (Cole [8])*

			Heuer [4]	
	Stanton [6] (from Literature), %	Colp and Ginzberg [7] (Own Cases), %	1,000 Cases (Own), %	36,623 Cases (from Literature), %
Peritonitis	15.4	16.5	37	33
Shock	5.0	...	..	..
Pneumonia	10.6	9.3	25	20
Pulmonary embolus	6.6	2.0	..	..
Cardiac failure	6.8	3.1	10	12
Renal failure	4.8	3.1	..	..
Operative hemorrhage	6.4	3.1	..	..
High temperature	4.0	...	..	..
Cholemia	4.4	...	..	..
Cholemia with hemorrhage	4.0	...	..	..
Hepatic insufficiency	3.8	...	..	4
Sepsis	3.2	3.1	..	..
Evisceration	0.2	3.1	..	..
Suppurative cholangitis	4.0	14.4	..	..
Pylephlebitis	...	8.2	..	..
Pancreatitis	...	5.2	..	2
Injury or stricture of the common duct	...	9.3	..	..
Gangrene or perforation	...	...	11	10
Miscellaneous	...	...	17	19

Infection and peritonitis were the most important causes of death in the first ten year period but were less a factor in the last ten years.

Stanton [6] in a review of 500 cases involving the biliary tract in which death followed operation and in which postmortem examination had been carried out, classified the causes of death as follows: infection and peritonitis, 38.4 per cent; hepatic insufficiency, 22 per cent; cardiovascular disease, 12.8 per cent; shock and hemorrhage, 11 per cent, and pneumonia, 10.6 per cent. These are approximately the percentages as reported by Colp and Ginzberg [7] and by Heuer [8] (table 9 from an article by Cole [8]).

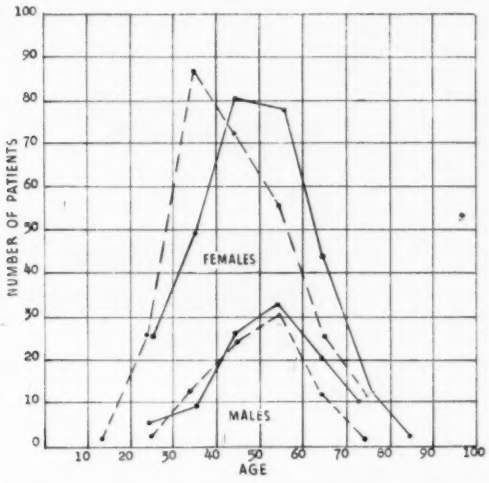


Fig. 2.—Age incidence of patients at the time of operation. Broken line is for the years 1927 to 1937 and solid line for the years 1937 to 1947.

Chart 2 is a graph of the peak age at the time of operation. The greatest number of men were between 50 and 60 years of age. This has remained the same throughout the two periods, but the age of the women has shifted from between 30 and 40 years to nearer 50 years. One would expect this to reflect adversely on the mortality statistics.

6. Stanton, E. M.: Immediate Causes of Death Following Operations Upon the Gall Bladder and Ducts, Am. J. Surg. **8**:1026 (May) 1930.

7. Colp, R., and Ginzberg, L.: Mortality in Surgical Diseases of the Biliary Tract, Ann. Surg. **105**:9 (Jan.) 1937.

8. Cole, W. H.: Factors in the Prognosis and Mortality of Gall Bladder Disease, Internat. Abstr. Surg. **69**:40 (July) 1939.

In chart 3 it is shown that acute infection of the gallbladder, hemorrhage, jaundice and involvement of the common duct, age and sex are all factors influencing mortality. Seventy and one-fifth per cent of the deaths in the first ten year period were in patients 50 years of age or over and 61.5 per cent in the second ten years. Hemorrhage, although a complicating factor in the last ten years, was not a significant influence in any fatality in this period, whereas it was in the first ten years. Thirty per cent of the deaths in the first ten years involved patients with acute cholecystitis and 12.5 per cent of those in the second ten year period. Fifty-six and three-fifths per cent of the patients who died in the first ten years were jaundiced and 75 per cent of those in the last ten year period; 40 per cent in the first ten year period were men and 50 per cent in the last ten years, whereas men comprised only 23.6 per cent and 27.3 per cent of the total cases in this series.

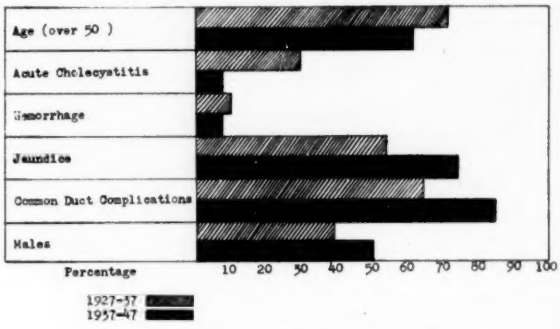


Fig. 3.—Factors contributing to mortality.

Cole,[8] in this regard, stated that whereas males were not as likely as females to have cholecystic disease, they were much more likely to have complications when it did develop.

SUMMARY

In this series the mortality in surgery of the biliary tract has been greatly reduced in the last ten years as compared with the preceding ten year period. This is noted particularly in the decrease in deaths due to infection and peritonitis.

The mortality of operation for uncomplicated chronic cholecystitis is lower than that of any other intra-abdominal procedure, but the rate rises rapidly when there are complications of the disease.

Age with its associated degenerative diseases, acute inflammation of the gallbladder or the ducts, hemorrhage, jaundice and complications involving the common duct contribute to the mortality.

ABDOMINAL OPERATIONS ON PATIENTS WITH CHRONIC PARAPLEGIA

Report of Cases

JACK GREENFIELD, M.D.
MEMPHIS, TENN.

THE LARGE number of patients with chronic paraplegia inherited by the United States from World War II are posing problems for every specialty in medicine and surgery. Some of these, such as patients with medical, neurosurgical, urologic, orthopedic and sociologic problems, those with decubitus ulcers and those with the problem of rehabilitation, have been dealt with in a number of publications.[1] Little has been mentioned of the problem of abdominal surgery,[2] which, though it occurs less often, is nevertheless important in the over-all management of the cases.

Patients with severe neurologic defects and anesthesia below the level of injury, with their ubiquitous medical and urologic complications and bed sores, tax the diagnostic acumen and the judgment of the surgeon

---

From the Surgical Service, Veterans Administration Medical Teaching Group, Kennedy Hospital.

Published with permission of the Chief Medical Director, Veterans Administration, who assumes no responsibility for the opinions expressed or the conclusions drawn by the author.

1. Freeman, W., and Heinburger, R. F.: The Surgical Relief of Spasticity in Paraplegic Patients: I. Anterior Rhizotomy, J. Neurosurg. **4**:435, 1947. Petroff, B. P.: War Wounds of Spinal Cord: The Paralyzed Patient; Urologic Aspects, J. A. M. A. **129**:154 (Sept. 8) 1945. Thompson, G. J.: Cord Bladder, Restoration of Function by Transurethral Operation, U. S. Nav. M. Bull. **45**:207, 1945. Munro, D.: The Rehabilitation of Patients Totally Paralyzed Below the Waist, With Special Reference to Making Them Ambulatory and Capable of Earning Their Own Living: III. Tidal Drainage, Cystometry and Bladder Training, New England J. Med. **236**:223, 1947. Munro, D.: Care of the Back Following Spinal Cord Injuries: A Consideration of Bed Sores, New England J. Med. **223**:391, 1940. Martin, J., and Davis, L.: Studies Upon Spinal Cord Injuries: I. The Development of Automatic Micturition, Ann. Surg. **126**:633, 1947. Conway, H.; Kraissl, C. J.; Clifford, R. H., III; Gelb, J.; Joseph, J. M., and Leveredge, L. L.: The Plastic Surgical Closure of Decubitus Ulcers in Patients with Paraplegia, Surg., Gynec. & Obst. **85**:321, 1947. Kostrubala, J. G., and Greely, P. W.: The Problem of Decubitus Ulcers in Paraplegics, Plast. & Reconstruct. Surg. **2**:403, 1947.

2. Hoen, T. I., and Cooper, I. S.: Acute Abdominal Emergencies in Paraplegics, Am. J. Surg. **75**:19, 1948.

who is called to see those among them who are suspected of having abdominal conditions. It is intended to discuss this phase of the paraplegic management and to present cases in which operation was performed by members of the surgical staff of the Kennedy Veterans Administration Hospital.

SYMPTOMS

Pain is a presenting symptom in the patients with acute abdominal conditions. The pain is usually poorly localized, dull and oppressing. Occasionally it may be sharp and recurrent. If the pain is sharp and knifelike with a radicular distribution, then the neurologic lesion must be ruled out as the cause of the pain. This is best done by consultation with the neurologist or the neurosurgeon. The next most common causes of abdominal pain in the paraplegic patients are urinary infection and calculi. Nausea and vomiting frequently accompany the pain in the urologic conditions. Because the patients practically always have cellular elements in the urine, urinalysis is usually of little help. Spasm and perforation of the bladder must be constantly borne in mind. Whenever there is the possibility of a urologic condition, consultation with the urologist is a must.

It is difficult to explain how these paraplegic patients perceive pain from the abdominal viscera. It seems that the abdominal viscera or at least their mesenteries are supplied with sensory nerve endings. The studies of Ray and Will indicate that in general the pain stimuli from the gastrointestinal tract are carried by the sympathetic fibers with the exception of the oral and distal colonic ends of the alimentary tract, which also have somatic pathways, and the bladder, which has parasympathetic as well as somatic pathways in addition to the sympathetic.[3] Conduction of painful sensation from the viscera to the spinal cord may be by way of the thoracic, splanchnic, hypogastric and pelvic nerves and thence over the posterior roots.[4] According to White, it is incorrect to consider the visceral sensory neurons as sympathetic nerve fibers, since they are mixed nerves containing a large preponderance of sympathetic motor fibers which belong to the posterior spinal root.[5] Although visceral sensation is conducted by the posterior root system similar to pain from the abdominal wall or the extremities, yet the pathways of reception of visceral sensory impulses and of somatic sensory impulses must be different, because many paraplegic patients with a physiologically complete division of the cord cannot perceive sensory somatic

3. Ray, B. S., and Neill, C. L.: Abdominal Visceral Sensations in Man, Ann. Surg. **126**:633, 1947.

4. White, J. C., and Smithwick, R. H.: The Autonomic Nervous System, New York, The Macmillan Company, 1945. Ray and Neill.[3]

5. White, J. C.: Sensory Innervation of the Abdominal Viscera Pain, Baltimore, Williams & Wilkins Company, 1944.

stimuli below the dermatome level of cord transection but can perceive painful stimuli from the viscera whose sensory fibers are believed to enter posterior roots below the level of division.[2] It has been noted that visceral pain satisfactorily relieved by bilateral cordotomy often gradually returns and that visceral pain pathways may have accessory pathways by which they reach the sensorium.[6] It has been suggested that visceral pain impulses may pass cephalad for several segments in the sympathetic ganglionic chain before entering the cord.[2] This could explain how pain is perceived in some cases, but does not explain the pain in all cases. Hoen and Cooper cited a quadriplegic patient with transection of the cord at the sixth cervical root who had sharp stabbing pain in the epigastrium due to gastric ulcer, the presence of which was confirmed by roentgenograms.[2] In such an instance, even the explanation that escape from injury of accessory pathways in the cord, represented by relays of short neurons close to the spinal gray matter,[7] is not satisfactory. It may be that in certain instances painful impulses from the stomach may be transmitted via the vagus nerves,[8] although Alvarez, among others, stated that vagotomy does not interrupt pain pathways from any of the viscera.[9] Fortunately the paralysis is incomplete in some cases, and in these the perception of pain may be no problem.

Because of flaccidity or spasticity, abdominal rigidity may be absent or unrecognizable, but a slight sense of resistance has been noticed with underlying infection.

Tenderness is not common in these patients but has been elicited, and when present it is of significance. In a paraplegic patient with a ruptured bladder tenderness was elicited in the suprapubic region.[2]

Nausea and vomiting are usually present in cases of acute abdominal conditions but can be misleading because paraplegic patients become nauseated and vomit more commonly from various causes than nonparaplegic patients. Nausea and vomiting are common with the urinary infections and urinary calculi, which the majority of these patients have at one time or another. Likewise, anorexia is so common that it becomes of no diagnostic value, unless it is a noticeable change from the previous condition.

Elevation of temperature is common in the paraplegic patient. A sudden rise to 103 F. or over is usually indicative of urinary sepsis. Sudden rises to lower temperatures occur in patients with acute abdomi-

6. Livingston, W. K.: Pain Mechanisms, New York, The Macmillan Company, 1944.

7. Karpus, J. P., and Kreidl, A. E.: Ein Beitrag zur Kenntnis der Schmerzleitung in Rückenmark, Arch. f. d. ges. Physiol. **158**:275, 1914.

8. Hoen and Cooper.[2] White and Smithwick.[4] Livingston.[6]

9. Alvarez, W. C.: Therapeutic "Information Please," Gastroenterology, J. A. M. A. **132**:970 (Dec. 21) 1946.

nal conditions and in those with phlebothrombosis. Elevation of the white blood cell count is of value only if a recent count has been made which could be used as a base line. A rapid pulse may give an important lead to a correct diagnosis of the acute abdominal condition.

Absence of intestinal sounds is only of value if it is known that they were present previously. Constipation and distention is so common in the otherwise "healthy" paraplegic patient as to be of no value in diagnosis. Likewise, air-filled, dilated intestinal loops are so frequent in ordinary patients with paraplegia that they are of no diagnostic value when seen on a roentgenogram of the abdomen. On the other hand, when fluid levels are seen, they have the usual significance. Demonstration of calculi in flat roentgenograms and in pyelograms in a case in which they were not previously present is of great help. After operative procedures, such as resection of the neck of the bladder, distention and ileus may be distressing to the uninitiated. Intestinal intubation with Wangensteen suction and enemas will frequently relieve the situation in a short time.

Fecal impaction should not act as a pitfall in diagnosis. Often the rectal examination, with removal of a hard bolus, will relieve all concerned, including the patient.

Jaundice has been more common in the paraplegic patients than in others. It is not known as yet whether this is due to the infectious hepatitis or to the transfusions of blood and plasma which most of them have received. Liver function studies, roentgenograms of the abdomen and cholecystograms may indicate whether biliary obstruction is the cause.

The diagnosis of acute trauma of the abdomen is made as in the normal person with the added handicap of the possibly absent tenderness, rigidity or localizing pain discussed previously. Referred pain may be of aid in diagnosis, as in the case of the ruptured spleen, presented later.

In addition to the acute abdominal conditions, there are others which require decisions on the part of the general surgeon. For example, the paraplegic patient with spasticity who has an inguinal hernia should have it repaired to avoid strangulation, although this complication has not been observed in the cases presented here.

Recognition of complications of abdominal surgery, such as subphrenic abscess, peritonitis and phlebothrombosis, requires a greater awareness on the part of the surgeon than is generally the case. In dealing with paraplegic patients he must "look for trouble," for reasons already discussed.

REPORT OF CASES

CASE 1.—F. K., a 29 year old white man, was injured on Oct. 11, 1946, which resulted in a fracture of the twelfth thoracic vertebra, with anterior displacement

of the eleventh and twelfth thoracic vertebrae, and paralysis, atrophy and complete anesthesia and analgesia below the eleventh thoracic dermatome anteriorly and posteriorly. Deep pressure was present down to the groin areas bilaterally. Vibration sense was present over the iliac spine. The upper abdominal reflexes only were present. He had paralysis, with incontinence of the bladder, for which a suprapubic cystotomy was performed. In addition he had deep ulcers over both trochanters. His usual white blood cell count was 3,000 to 4,000. Routine urinalysis done in July and on Aug. 15, 1947 revealed no abnormalities.

On August 16 the patient complained of pain in the right lower quadrant. Tenderness was present. The white blood cell count was 6,550 with 52 per cent polymorphonuclear cells. Urinalysis showed 25 to 30 white blood cells, with a few red blood cells. Observation was decided on. On August 17 the temperature was 98.8 F., the tenderness in the right lower quadrant was more marked and some rebound tenderness was present. The patient was nauseated. The results of rectal examination were negative. The white blood cell count had risen to 8,400. In spite of the change in the urine, the surgeon who saw the patient elected to perform appendectomy for fear of neglecting acute appendicitis. The appendix was removed. It "did not look too bad." There was no Meckel diverticulum or enlarged lymph nodes in the mesentery. The pathologic report stated: "This section of appendix shows considerable fibrosis of the entire appendical wall, and there is some infiltration, especially of the serosal layer, with chronic inflammatory cells. The mucosa is almost entirely absent, and the lumen is filled with cellular debris and amorphous acidophilic material."

The postoperative course was uneventful. The sutures were removed on the fifth postoperative day. Although he has had no recurrence of the abdominal pain, nausea or relative leukocytosis since operation, he has had several instances of recurrence of cellular elements in the urine until the time of this writing, in March 1948.

Case 2.—S. R., a 22 year old white man, suffered a fracture of the ninth thoracic vertebra on Aug. 29, 1945, which resulted in paralysis of the lower extremities, the sensory level at the tenth thoracic dermatome, and loss of bladder and rectal control. A urethral catheter was kept in place for bladder control. He was admitted to the Kennedy Veterans Administration Hospital on Aug. 24, 1946, with decubitus ulcers of the sacrum, hips, thighs, ankles and heels in addition to the aforementioned condition. Because of spasm, rhizotomy was performed on Sept. 10, 1946, including the anterior roots of the eleventh thoracic through the first sacral nerves and the posterior roots of the eleventh thoracic through the first lumbar nerves. Subsequently, acute pyelonephritis developed, which was successfully treated with penicillin and sulfadiazine. On Oct. 26 and Nov. 2, 1946, stones were removed from the bladder by cystoscopy. In the latter part of November 1947 another acute urinary infection occurred, which responded to penicillin. A dermanaplastic closure of the ulcer on the left side of the ischium was done on December 30 and redone on Jan. 30, 1947. On May 1, 1947, grafts were placed on the ulcers on the sacrum and the right trochanter.

On August 3 he began to complain of dull pain in the right lower quadrant. He had a white blood cell count of 10,000, with 72 per cent polymorphonuclear cells, slight elevation of the temperature and 10 to 20 white blood cells in the urine. Appendectomy was performed after several examinations revealed deep tenderness in the right lower quadrant. The pathologic report was lymphoid hyperplasia. The patient had no further bouts of pain.

In both instances the urologist, had he been called, could have corrected the complaints by treating the urinary infection. The surgeon was led to appendectomy in both of these cases, without acute appendicitis, because of the complaint of pain, the persistent tenderness and the elevated white blood cell count. It is difficult to criticize the removal of a nonsuppurative appendix in these cases when nonremoval of a suppurative appendix might lead to unrecognized perforation with its sad sequelae.

It has been a somewhat unexpected occurrence that in an average population of about 200 paraplegic patients at this hospital there have been no recognized instances of acute appendicitis in over one and one-half years of observation. Neither have any of the patients had peritonitis, which might have indicated inability to diagnose the condition.

CASE 3.—F. A., a 22 year old white man, suffered a fracture of the sixth cervical vertebra, with paralysis from the arm down, including the bowel and bladder, on Oct. 3, 1945, while wrestling and practicing jiu-jitsu. He was admitted to the Kennedy Army General Hospital on October 4. After traction, he could move his right arm somewhat. He improved gradually until he could move his legs and control urination with a condom-type apparatus by November 25 (automatic bladder). On Jan. 5, 1946, he was transferred to the Kennedy Veterans Administration Hospital. Examination showed chronic traumatic transverse incomplete myelitis, at the level of the first thoracic segment. In May 1946 he began to use his legs without a brace and was able to void without a catheter or the use of the condom some of the time. He required enemas for evacuation of the bowels. At no time did decubitus ulcers or urinary calculi develop.

On Nov. 4, 1947, he had an elevation of temperature to 100 F. and felt chilly. Subsequently he had similar elevations of temperature. The urine was normal. The lungs were clear. On November 18 a routine examination of the kidney, ureter and bladder showed no urinary calculi, but there were stones in the gallbladder. The white blood cell count at this time was 6,600 with 64 per cent polymorphonuclear cells. The prothrombin time was normal. An oral cholecystogram showed calculi in the gallbladder and the cystic duct. He had no pain during this period, and tenderness was not elicited. He had the common food likes and dislikes seen among paraplegic patients. There was no nausea or vomiting. Stools were of normal color. There being no other explanation of the fever, it was decided to do a cholecystectomy.

Cholecystectomy was done on Jan. 5, 1948, with the patient under cyclopropane anesthesia through a right rectus incision. Since the cholecystectomy was a simple one, routine appendectomy was done at the same time, and the gallbladder bed was drained. The common duct was found to be normal. There was a calculus in the cystic duct. The pathologic diagnosis was chronic cholecystitis with cholelithiasis and obliterative appendicitis. The drain was removed on the second postoperative day. The sutures were removed on the seventh postoperative day. An abdominal binder was used until the fifteenth postoperative day. Healing was per primum and uneventful. On the twenty-second day the patient was taken off the low fat diet and given the regular diet and routine daily enemas and placed on the rehabilitation program which he had been following prior to operation. When last seen, in March 1948, he was still afebrile.

CASE 4.—W. R., a 56 year old white man, suffered an injury to his right hip region in 1941, which left his right lower extremity weak. In 1944, while at work, he suddenly suffered paralysis of the lower half of the body, with numbness. In 1945 a laminectomy was performed and an epidural granuloma was removed from the region of the fifth thoracic vertebra. When he was admitted in 1947, studies revealed adhesive chronic arachnoiditis involving the fourth through the ninth thoracic segments due to epidural granuloma; transverse, chronic, incomplete, secondary myelitis, with paraplegia below the third thoracic segment and partial paralysis of the bowel and bladder, and psychoneurosis of the mixed type, with personality changes due to emotional instability and anxiety.

Beginning in June 1947, he complained of pain in the right upper quadrant, with radiation to the right scapula, along with many other aches and pains over the entire body, which were considered to be on a psychoneurotic basis. The pain in the right upper quadrant was often accompanied with pain in the left upper quadrant, which radiated much like symmetric root pain. In other words, his pain was difficult to evaluate. Neurologic, cardiac, colonic and genitourinary changes were ruled out by progressive studies and consultations. Four attempts at visualization of the gallbladder by the oral administration of priodax® (iodoalphionic acid N.N.R.) failed. His sensory level was complete just below the nipple line. In March 1946, because of the radiating pain and the nonfilling after dye was given orally, it was finally decided that he must have a diseased gallbladder, although localized tenderness or palpable viscus was not present. A history of intolerance to fatty foods could be elicited only to a minor degree. He did have belching and flatulence frequently. On many occasions he vomited, especially when he was emotionally upset.

On March 3, 1946, a celiotomy was done through a right rectus incision with the patient under anesthesia produced by cyclopropane given endotracheally and curare. A chronically inflamed gallbladder packed with cholesterol stones was found. The wall seemed thinned out by the numerous calculi. The common duct appeared normal. The gallbladder was removed, the bed of the viscus was drained and closure was performed in layers. Convalescence was uneventful. He was relieved of the pain and tenderness in the right upper quadrant, the belching and the flatulence, and he resumed his rehabilitation program.

It is felt by the surgical staff at this institution that the paraplegic patient with cholelithiasis should undergo cholecystectomy, even if the symptoms are mild, to avoid perforation or obstructive jaundice which might be difficult to recognize or to differentiate from hepatitis later. Because of the frequent association of cholecystitis with appendicitis, it is felt that when the cholecystectomy is a simple one, the appendix should be removed.

In case 3, because no other cause for the fever was found and to avoid later complications mentioned previously, it was decided to perform cholecystectomy although there was no pain or tenderness.

The psychoneurotic element, the bilateral pain and the absence of localized tenderness in case 4 were misleading, but, with suspicion aroused, the repeated nonfilling of the gallbladder after administration of dye finally led to cholecystectomy for a definitely diseased gallbladder.

CASE 5.—G. J., a 40 year old white man, fell down a flight of stairs on June 11, 1943, suffering cerebral concussion and fracture of the eleventh thoracic vertebra, resulting in complete motor and sensory paralysis below the level of the eleventh thoracic dermatome. Decubitus ulcers developed, and he had several attacks of pyelitis. Enemas were used for evacuation of the bowels, and urethral catheter with irrigations for control of the bladder.

Beginning in August 1945, he complained of pain in the lower abdominal area. This was not relieved by a chordotomy performed in 1946. In May 1947, shortly after an investigative cystoscopic examination, the pain became localized in the left lower quadrant, and he began to have mucopurulent, foul-smelling drainage from the rectum. His temperature rose to 100 or 101 F. daily. There was tenderness in the left lower quadrant. The results of examination after a barium enema were negative. The stools did not contain occult blood, amebas, ova or parasites. Proctosigmoidoscopic examination was noncontributory. The surgeon felt that there was an abscess in the left lower quadrant, possibly due to diverticulitis and recommended drainage. Further therapy with penicillin and streptomycin was elected, however. By June 10, 1947, a definite mass could be felt in the left lower quadrant laterally which was tender to palpation.

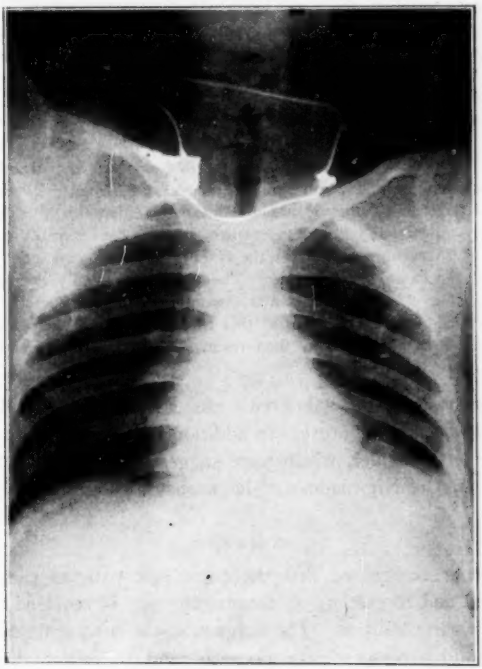
On June 24, 1947, exploration through a large left McBurney incision was done; inhalation anesthesia was used. A large abscess lateral to the sigmoid was found and drained. No evidence of the suspected diverticulitis was found. At no time was there any fecal drainage from the wound. His temperature rapidly became normal and the purulent drainage from the anus ceased. On July 7 the sutures in the skin were removed. Drainage from the incision gradually subsided and ceased, and the drain was removed. By July 22 he was well healed. Rehabilitation and treatment of his recurrent urinary infection and decubitus ulcers then proceeded as usual. A check barium enema revealed no diverticula or any other pathologic process, and pyelograms were normal. He has maintained this status to the time of this report, in March 1948.

The fever, the mucopurulent drainage from the rectum and the tenderness in the left lower quadrant in the absence of demonstrable ureteral calculus or lesion of the colon led the surgeon to suspect, correctly, the presence of pus under the area of tenderness. This patient feared carcinoma in spite of the assurance given after proctoscopic examination and study of the colon with barium gave negative results. The exploratory incision and the adequate drainage of the abscess relieved his mind and the condition causing symptoms.

CASE 6.—Z. J., a 25 year old white man, was struck by shell fragments in the spine on June 16, 1944, which resulted in complete transverse myelitis at the level of the tenth thoracic dermatome. Grafts were placed on a sacral ulcer in March 1945 and again in August 1945, finally resulting in healing. On Jan. 22, 1946, the suprapubic cystotomy opening was closed. In December 1945 chordotomy (second thoracic vertebra) was performed for pain.

While driving a "paraplegic automobile" on Aug. 13, 1947, the patient had an accident. He was brought to the hospital two hours later in a semiconscious state with lacerations about the face. Bowel sounds were diminished but present. Anesthesia was present below the tenth thoracic vertebra as before. There was no muscle spasm or rigidity, nor was there any distention. There was an obvious fracture of the right tibia. The knee region on both legs exhibited abnormal

mobility. There were numerous abrasions about the lower extremities. The blood pressure was 70 systolic. No diastolic pressure was elicited. The pulse was 140 per minute and the respiratory rate was 30 per minute. He was given 500 cc. of plasma and 500 cc. of citrated blood intravenously. His blood pressure fell to 50 systolic and 25 diastolic, and shifting dulness was elicited in the flanks. He complained of bilateral pain in the shoulder at this time. The abdomen became more tympanitic in the upper half, and the patient complained of severe thirst. At this time the temperature had risen to 104 F. Roentgenograms taken at the



Roentgenogram of chest, Aug. 24, 1947, showing elevation of the left side of the diaphragm in case 6.

bedside showed an oblique fracture through the shaft of the left tibia about 10 cm. from the knee joint. There were bilateral supracondylar impacted fractures through the distal ends of both femurs, with 1.5 cm. impaction on both sides.

In addition to the time taken for restorative measures there was several hours' delay in diagnosis because of the lack of local signs of intra-abdominal trauma and the lack of localizing tenderness and rigidity. However, the shock, the rapid pulse and the onset of pain in the left shoulder, which persisted after restorative measures were tried, along with the beginning distention and the shifting dulness led the surgeon to the conclusion that there was intra-abdominal bleeding, most probably from the spleen and less probably from torn mesentery.

Laparotomy was performed without anesthesia through a transverse incision in the upper abdominal area, at 5 a. m. Because of protrusion of the bowel in the wound, nitrous oxide-oxygen-ether anesthesia was started. Two thousand cubic centimeters of bloody fluid was aspirated from the peritoneal cavity. The spleen was lacerated at the hilus and contained a large subcapsular hemorrhage. It was removed. Closure was performed in layers with chromic surgical gut for the peritoneum and wire for the outer layers. Casts were applied to both lower extremities.

On the following day the distention seemed controlled by the Levine tube which had been inserted. Each day his temperature rose as high as 103 F. The urine was normal, and the ouput was good. He began to have diarrhea. The pulse rate increased gradually to 120 per minute and the leukocyte count was 27,000, with a shift to the left in the Schilling hemogram. The patient complained of pain in the left shoulder region. A roentgenogram showed the left leaf of the diaphragm to be elevated (figure). It was decided that he had a subphrenic abscess, and he was treated with streptomycin.

On Aug. 26, 1947, a portion of the tenth rib was resected posterolaterally and a pack placed against the diaphragmatic pleura. On August 29 the pack was removed and a large subphrenic abscess drained. After this the distention and diarrhea were alleviated. The temperature and the pulse rate gradually fell. On September 26 roentgenograms of the fracture sites showing good callus were obtained, and the casts were removed. The abscess gradually decreased in size, the administration of streptomycin was discontinued and by October 14 he was completely healed. Roentgenograms at this time showed the chest and diaphragm to be normal. Rehabilitation was then resumed and was being continued at the time of writing.

The diagnosis of the subphrenic abscess was more readily arrived at than that of splenic rupture. In addition to the fever and the referred pain in the left shoulder, which were suggestive, the elevated diaphragmatic leaf on the left made the diagnosis of subphrenic abscess conclusive.

COMMENT

It is being recognized that the paraplegic patients cannot be put away in bed and forgotten. Constant diligence is required to discover changes in their condition. The surgeon's role is to evaluate the signs, symptoms and accessory data properly and to follow through with adequate action based on good judgment. Complaints and changes in clinical status may be investigated by examinations and roentgenologic and laboratory studies as in other patients. The experience obtained from this small group of cases as well as from others in which colostomy and colostomy closure were done for traumatic abdominal conditions seems to indicate that the patients withstand abdominal surgery well and that healing progresses as usual, providing nutrition, fluid balance and circulating blood elements are kept within normal limits by the usual methods.

No doubt there will be other abdominal conditions arising which will require thought and action on the part of the general surgeon. It is

the practice of the paraplegic service at this hospital to make periodic surveys of these patients, including flat roentgenograms of the abdomen, blood counts and urinalyses. All patients are kept on adequate diets and urinary infection and calculi are kept at a minimum with the use of acidification, antibacterial agents, ambulation and surgical intervention. The surveys act as a base line for changes when complaints develop which require surgical judgment. Unquestionably, it is difficult, even with this help, to be as certain as with normal subjects.

SUMMARY

Signs and symptoms of abdominal conditions requiring surgical treatment in patients with chronic paraplegia are discussed.

Two cases involving the appendix, 2 cases of cholelithiasis, 1 of perisigmoid abscess and 1 of a traumatic spleen complicated by a postoperative subphrenic abscess are presented.

Routine clinical and laboratory surveys as well as diligent "search for trouble" are valuable in determining abdominal conditions in patients with chronic paraplegia.

Experience with this small group of cases seems to indicate that patients with chronic paraplegia withstand abdominal operations well and heal as quickly as others do.

ADENOMATOUS GOITERS WITH AND WITHOUT HYPERTHYROIDISM

Some Aspects of the Relationship of the Microscopic Appearance to Hyperthyroidism

JAMES R. JOHNSON, M.D.
Fellow in Surgery, Mayo Foundation
ROCHESTER, MINN.

THE DATA presented herein are drawn from a larger study. The general purpose of the complete study was to determine if possible whether any histologic data can be found on the adenomatous nodules of the thyroid gland which would correlate with the presence of thyrotoxicosis in a patient. In short, it was decided to inquire again into the question of whether the pathologist can predict the presence of toxic phenomena in the patient from examination of the nodular or adenomatous tissue from the thyroid gland.

A nodule of the thyroid gland may be defined as a more or less encapsulated mass of thyroid tissue which may or may not be different from the surrounding thyroid tissue.

The term "nodular goiter" is used frequently by pathologists and surgeons as a synonym for adenomatous goiter. Although it is true that adenomatous goiters are nodular, thyroid nodules are not necessarily adenomas. Thyroid nodules may be composed of apparently normal thyroid tissue, colloid, inflammatory or lymphoid tissue, adenomas or carcinomas (figs. 1 and 2).

THE ADENOMA

Adenomas of the thyroid gland are encapsulated and differ macroscopically and microscopically from the surrounding thyroid tissue. Adenomas may be single or multiple and may be associated with hyperthyroidism, with normal or reduced thyroid function or with exophthalmic goiter. They tend to undergo degeneration, such as necrosis, hemorrhage, fibrosis, hyalinization, calcification, formation of cysts and lipoidosis. Degenerative changes are more marked in the adenoma than in the extra-adenomatous thyroid tissue.

Adenomas usually contain follicles of fetal type and larger follicles containing colloid. However, the cells may appear (1) in diffuse

---

Abridgment of thesis submitted by Dr. Johnson to the Faculty of the Graduate School of the University of Minnesota in partial fulfillment of the requirements for the degree of M.S. in Surgery. Work was done under the supervision of Dr. A. C. Broders Sr.

masses without formation of follicles (undifferentiated fetal adenoma); (2) in small follicles of fetal type with small lumens which contain no colloid (fetal adenoma); (3) in follicles of fetal type with larger lumens and a small colloid content, or (4) in well developed follicles lined by cuboid or columnar epithelium and with large lumens filled with colloid (fetal and colloid adenoma).[1] Unencapsulated nodules which consist only of thyroid tissue containing colloid are not regarded as true adenomas but as part of a colloid goiter.

Opinions differ about the microscopic appearance of thyroid adenomas removed from patients with clinical manifestations, which H. S. Plummer[2] designated adenomatous goiter with hyperthyroidism.

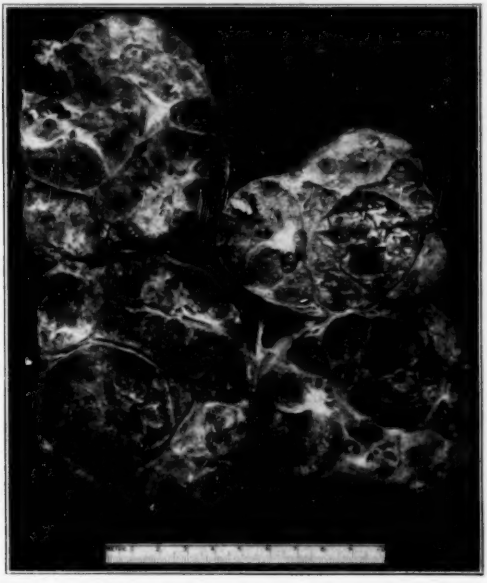


Fig. 1.—Multiple well encapsulated adenomas of the thyroid.

Broders[3] has stated that the amount and height of the columnar epithelium in the adenomas (parenchymatous hypertrophy) probably

1. Broders, A. C., and Parkhill, E. M.: Symposium on Surgical Lesions of Thyroid: Diffuse and Adenomatous Goiter and Goiter Induced by Various Agents, Surgery **16**:633-646 (Nov.) 1944.

2. Plummer, H. S.: The Clinical and Pathologic Relationships of Hyperplastic and Non-Hyperplastic Goiter, J. A. M. A. **61**:650-651 (Aug. 30) 1913.

3. Broders, A. C.: Personal communication to the author; Surgical Pathology of the Thyroid Gland, West. J. Surg. **48**:620-632 (Oct.) 1940. Broders and Parkhill.[1]

determine the activity of thyroid adenomas. In order to make a diagnosis of adenomatous goiter with hyperthyroidism on microscopic examination he requires that the extra-adenomatous thyroid tissue be practically normal or at least not show the microscopic features of exophthalmic goiter.

Broders [3] has found that intra-adenomatous columnar epithelium, with or without papillary infolding, appears most often in adenomas associated with exophthalmic goiter, less often in adenomas associated with hyperthyroidism and rarely or perhaps one should say least often, in adenomas from patients with normal thyroid function.

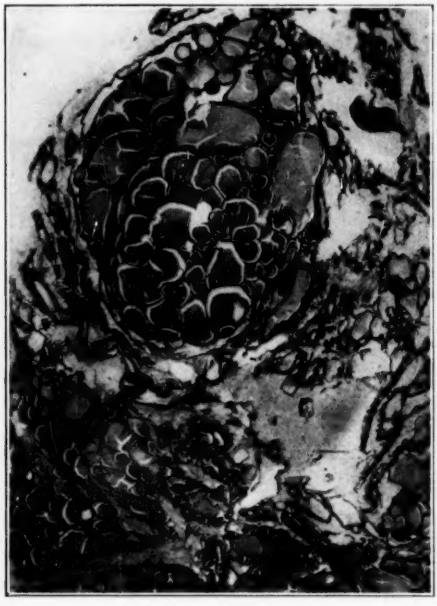


Fig. 2.—Small noncapsulated colloid nodule from a thyroid gland, not an adenoma; × 13.

Welch and Broders [4] studied the Golgi apparatus in the thyroid glands of 73 patients. Thirty-five of the patients had exophthalmic goiter, 21 adenomatous goiter with clinical hyperthyroidism, 16 adenomatous goiter in which clinical hyperthyroidism was not evident and 1 colloid goiter. Of the 35 glands examined from patients with exophthalmic goiter, 34 showed hypertrophy of the Golgi apparatus. Of

4. Welch, C. S., and Broders, A. C.: Golgi Apparatus of the Thyroid Gland, Arch. Path. **29**:759-772 (June) 1940.

the 21 adenomatous thyroid glands examined in which the patients had clinical hyperthyroidism, only 7 had intra-adenomatous cellular hypertrophy, whereas 19 had a hypertrophied Golgi apparatus, which led the authors to suggest that the size of the Golgi apparatus is a more delicate method of estimating cellular function than the usual histologic one. Of the 16 adenomatous thyroid glands from patients who did not have clinical evidence of hyperthyroidism, only 1 showed intra-adenomatous cellular hypertrophy and 5 showed hypertrophy of the Golgi apparatus. In colloid goiter the Golgi apparatus was not enlarged.

Before the use of iodine in the treatment of hyperthyroidism, Wilson [5] studied a large number of adenomatous goiters without diffuse extra-adenomatous parenchymatous hypertrophy and hyperplasia. He found that in 90 per cent of the group in which a clinical diagnosis of hyperthyroidism was made, small areas of either intra-adenomatous or extra-adenomatous hypertrophy and hyperplasia were present. In 95 per cent of the nonhyperthyroid group, no areas of parenchymatous hypertrophy and hyperplasia were found. The hypertrophy and hyperplasia were often so moderate in degree and amount as to escape notice except by careful inspection. The most pronounced evidence of hypertrophy and hyperplasia in adenomatous goiter with hyperthyroidism was comparable to that in untreated exophthalmic goiter of the mildest degree.

Rice [6] stated that the histologic diagnosis of adenomatous goiter with hyperthyroidism is an uncertainty. Only 58 per cent of the adenomas with hyperthyroidism that he examined showed evidence of parenchymatous hypertrophy and hyperplasia.

A number of writers have found it impossible microscopically to distinguish between thyroid adenomas with hyperthyroidism and those without it.[7] Although formerly hypertrophy and hyperplasia in the

5. Wilson, L. B.: A Study of the Pathology of the Thyroids from Cases of Toxic Non-Exophthalmic Goiter, Am. J. M. Sc. **147**:344-351 (March) 1914; The Pathology of Nodular (Adenomatous?) Goiters in Patients With and in Those Without Symptoms of Hyperthyroidism, Am. J. M. Sc. **165**:738-742 (May) 1923.

6. Rice, C. O.: Exophthalmic Goiter Versus Toxic Adenoma: Clinical and Pathologic Differential Features, Minnesota Med. **17**:361-365 (June) 1934.

7. (*a*) Marine, D., and Lenhart, C. H.: The Pathological Anatomy of the Human Thyroid Gland, Arch. Int. Med. **7**:506-535 (April) 1911. (*b*) Graham, A.: Exophthalmic Goiter and Toxic Adenoma: Clinical Variations of the Same Disease, J. A. M. A. **87**:628-631 (Aug. 28) 1926. (*c*) Marine, D., and Lenhart, C. H.: On the Occurrence of Goitre (Active Thyroid Hyperplasia) in Fish, Bull. Johns Hopkins Hosp. **21**:95-98 (April) 1910. (*d*) Rienhoff, W. F., Jr., and Lewis, D.: Relation of Hyperthyroidism to Benign Tumors of the Thyroid Gland, Arch. Surg. **16**:79-116 (Jan.) 1928. (*e*) Bovi, E. J. D.: Thyroid Gland: A Clinical Pathologic Study with Special Reference to True Tumor: Analysis of Two Hun-

(Footnote continued on next page)

thyroid have often been taken as evidence of hyperfunction, certain goitrogenic substances, for example cabbage, potassium thiocyanate, sulfonamide drugs and thiouracil, have been shown to produce notable degrees of hypertrophy in the thyroid, with diminished thyroid function.[8] While the effect of such substances on the microscopic appearance of thyroid nodules has not been fully established, it must be kept in mind in any consideration of the significance of hypertrophy of thyroid cells.

Adenomatous goiters may occur in cretins, and Hertzler[9] designated them as bosselated congenital goiters. "Cross section of these degenerated goiters presents a general pattern of diffuse, small cystic degeneration with multiple fetal adenomatosis. The microscopic picture varies. For the most part, there is an absence of colloid. Usually the epithelium is cuboid."

MATERIAL STUDIED AND METHOD

For this study material was obtained at necropsy and at operation on the thyroid gland. The necropsy material consisted of 165 thyroid glands. These were completely removed at necropsy during a six month period at the Mayo Clinic. In each case the patient died of a disease not primarily related to the thyroid gland. The surgical material consisted of 58 adenomatous goiters without hyperthyroidism and 115 adenomatous goiters with hyperthyroidism. These goiters were selected from a consecutive group, surgically removed. All cases of carcinoma of the thyroid were excluded from the surgical series. In each of the 58 cases a consultant in the Section on Metabolism of the Mayo Clinic had made a clinical diagnosis of adenomatous goiter without hyperthyroidism, and in each of the 115 cases one had made a clinical diagnosis of adenomatous goiter with hyperthyroidism.

---

dred and Sixteen Cases, Arch. Surg. **39**:624-636 (Oct.) 1939. (*f*) Warwick, M.: The Pathology of Toxic Goiter, Minnesota Med. **10**:411-412 (July) 1927. (*g*) Enzer, N.: The Pathology of Nodular Goiter, Ann. Int. Med. **3**:1241-1251 (June) 1930. (*h*) Boyd, A. M.: The Pathology of Single Nodule of the Thyroid Gland, Brit. J. Surg. **25**:782-789 (April) 1938.

8. Chesney, A. M.; Clawson, T. A., and Webster, B.: Endemic Goitre in Rabbits, Bull. Johns Hopkins Hosp. **43**:261-277 (Nov.) 1928. Rawson, R. W.; Hertz, S., and Means, J. H.: Thiocyanate Goiter in Man, Ann. Int. Med. **19**:829-842 (Dec.) 1943. Webster, B., and Chesney, A. M.: Endemic Goitre in Rabbits, Bull. Johns Hopkins Hosp. **43**:291-308 (Nov.) 1928. MacKenzie, C. G., and MacKenzie, J. B.: Effect of Sulfonamides and Thiourea on the Thyroid Gland and Basal Metabolism, Endocrinology **32**:185-209 (Feb.) 1943. Astwood, E. B.; Sullivan, J.; Bissell, A., and Tyslowitz, R.: Action of Certain Sulfonamides and of Thiourea on the Function of the Thyroid Gland of the Rat, Endocrinology **32**:210-225 (Feb.) 1943. Marine and Lenhart.[7c] Rienhoff and Lewis.[7d] Bovi.[7e]

9. Hertzler, A. E.: Diseases of the Thyroid Gland Presenting the Experience of More than Forty Years, New York, Paul B. Hoeber, Inc., 1941.

The surgical series was carefully selected in order to exclude any gland in which the extra-adenomatous parenchymatous hypertrophy was more than grade 1. The basis of grading will be described later. This selection was made in order to find out whether in adenomatous goiters the grade of intra-adenomatous parenchymatous hypertrophy correlated with the presence and degree of hyperthyroidism.

The age and sex of each patient whose thyroid was studied, the weight of each thyroid gland, the presence of nodules and adenomas, the microscopic appearance of the thyroid, the presence and grade of intra-adenomatous and extra-adenomatous parenchymatous hypertrophy and the significant clinical and pathologic findings were recorded. Each thyroid was sectioned every 2 to 3 mm. on gross examination in a search for adenomas. Other details in the study and selection of necropsy and surgical material were as follows: Blocks from the 58 surgically removed thyroids were embedded in paraffin; sections were taken from each block and stained with hematoxylin and eosin.

In a few instances the adenoma was largely calcified, and it was possible to get only a few sections. When extra-adenomatous tissue was present, sections were made of this to rule out diffuse parenchymatous hypertrophy.

The 115 surgically removed thyroids in cases in which the clinical diagnosis of adenomatous goiter with hyperthyroidism was made and the 165 thyroids removed at necropsy were sectioned in the same manner.

In this study, parenchymatous hypertrophy is defined as a change in the thyroid follicular cells from flat or cuboid epithelium to columnar epithelium. The extent of parenchymatous hypertrophy was graded from 0 to 4, grade 0 representing a gland with minimal or no columnar epithelium and grade 1 a gland with low columnar epithelium in at least several areas in a section. Grade 4 indicated the presence of diffuse high columnar epithelium, corresponding to the usual histologic picture in untreated exophthalmic goiter, and grades 2 and 3 were intermediate between grades 1 and 4 (figs. 3 to 6).

The grade of parenchymatous hypertrophy recorded was the highest found in any one section. A large number of sections was cut from each gland. A thyroid showing extra-adenomatous parenchymatous hypertrophy greater than grade 1 (on a basis of 1 to 4, in which 1 represents the least and 4 the greatest degree) was considered to be possibly an exophthalmic goiter and was therefore excluded from the surgical group.

OBSERVATIONS IN NECROPSY GROUP

Of the 165 thyroid glands removed at necropsy, 97 (58.8 per cent) were nodular. Forty-nine (50.5 per cent) of the nodular goiters were adenomatous goiters. The remaining nodules were found to be adult

thyroid tissue, colloid cysts, colloid nodules or inflammatory thyroid tissue. Three (6.1 per cent) glands in this group were substernal.

Age of Patients.—The average age of the 68 patients in this group who had apparently normal thyroid glands, that is, without nodules, was 51.8 years; the age of those who had nodular thyroids without adenomas was 57.1 years and of those who had adenomatous goiters 65.4 years. No adenomas were found in patients less than 20 years of age. In this group the incidence of nodular goiters seemed to increase with age.

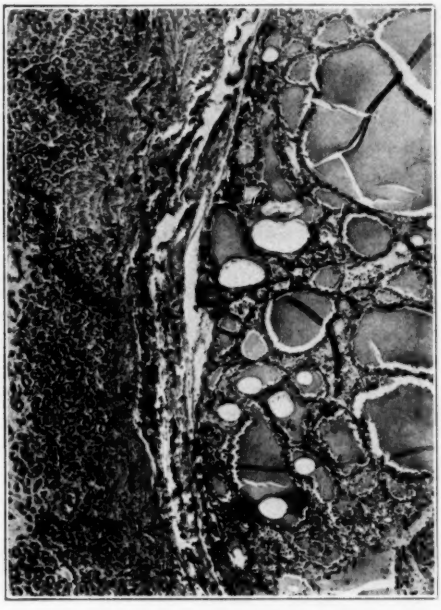


Fig. 3.—Two fetal and colloid adenomas of the thyroid gland separated by a fibrous capsule. Intra-adenomatous parenchymatous hypertrophy of grade 0; × 55.

Sex.—Of the 165 persons examined at necropsy, 115 were men. Sixty-six (57.4 per cent) of these had nodular goiters. Twenty-five (21.7 per cent of the men, or 37.9 per cent of the men who had nodular goiters) had adenomatous goiters. Of the 50 women in this group, 33 (66 per cent) had nodular goiters and 23 (46 per cent of the total number of women, or 70 per cent of the women with nodular goiters) had adenomatous goiters. The incidence of small thyroid nodules was about 10 per cent greater in women than in men, and the incidence of small adenomatous goiters was more than twice as high in women.

Weight.—The average weight of the thyroid glands without nodules removed at necropsy was 26 Gm. The weight varied from 5 to 61 Gm. The smallest thyroid was removed from a patient who had hypopituitarism. The average weight of the nodular thyroids without adenomas removed at necropsy was 28 Gm.; the weight ranged from 10 to 52 Gm. The average weight of the 49 adenomatous thyroids removed at necropsy was 48.5 Gm. The smallest, which was from a patient who previously had undergone subtotal thyroidectomy, weighed 8 Gm. and the largest 232 Gm.

Fig. 4.—Intra-adenomatous parenchymatous hypertrophy of the thyroid of grade 1; × 160.

Microscopic Observations.—Of the 49 adenomatous goiters encountered at necropsy, in 2 (4 per cent) unsuspected adenocarcinoma, grade 4, was found. In 15 (30.6 per cent) there was intra-adenomatous parenchymatous hypertrophy of more than grade 1. Some of these also showed extra-adenomatous parenchymatous hypertrophy. This may indicate the existence of exophthalmic goiter. Thirty-seven (75.5 per cent) showed degenerative changes, that is, hemorrhage, fibrosis, hyalinization, cyst formation, lymphocytic infiltration, deposits of cholesterol

crystals and lipoid granular degeneration. Four (8.2 per cent) were pure fetal adenomas. The other 45 (91.8 per cent) were fetal and colloid adenomas.

SURGICAL SERIES

The basal metabolic rate before operation ranged from — 20 to + 10 per cent in the 58 cases of adenomatous goiter without hyperthyroidism and from + 11 to + 93 per cent in the 115 cases of adenomatous goiter with hyperthyroidism. Three (5.2 per cent) of the adenomatous goiters

Fig. 5.—Intra-adenomatous parenchymatous hypertrophy of the thyroid of grade 2; × 160.

without hyperthyroidism in the surgical series were substernal and 8 (7 per cent) of the adenomatous goiters with hyperthyroidism were substernal.

Age of Patient.—The average age at the time of operation of the patients in this series who had undergone surgical resection of adenomatous goiters without hyperthyroidism was 47.5 years. For those who had had adenomatous goiters with hyperthyroidism surgically removed the average age was 51.4 years. There was no patient in this series less than 20 years of age with an adenomatous goiter.

Only 15 per cent of the patients who had undergone surgical resection of adenomatous goiters with hyperthyroidism were less than 40 years old. Five (8.6 per cent) of those with adenomatous goiters without hyperthyroidism were more than 60 years old, while 32 (27.8 per cent) of those with adenomatous goiters wth hyperthyroidism were more than 60. Of the patients who were more than 60 years old and had had adenomatous thyroid resected, 82.1 per cent had hyperthyroidism.

Sex.—Of the 58 adenomatous goiters without hyperthyroidism removed by subtotal resection, 51 (87.9 per cent) were from women. Of

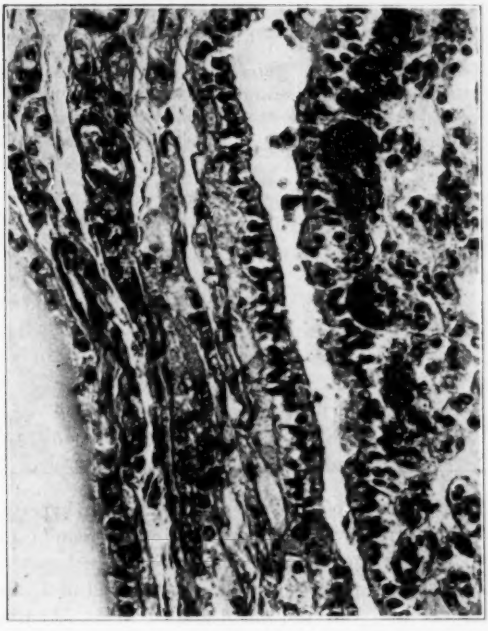


Fig. 6.—Intra-adenomatous parenchymatous hypertrophy of the thyroid of grade 2 to 3; × 360.

the 115 adenomatous goiters with hyperthyroidism surgically removed, 93 (80.8 per cent) were from women. In this series, therefore, adenomatous goiters of sufficient size or producing symptoms sufficient to bring the patient to operation were four to seven times as common in women as in men.

Weight.—The average weight of the surgically resected adenomatous goiters without hyperthyroidism was 88.7 Gm. The smallest amount of thyroid tissue removed was 13 Gm. and the largest amount 390 Gm.

The average weight of the surgically resected adenomatous goiters with hyperthyroidism was 92 Gm. The smallest amount of thyroid tissue removed was 16 Gm. and the largest amount 632 Gm.

Microscopic Observations.—That degenerative changes are common in thyroid adenomas is shown by their occurrence in 100 per cent of those removed surgically. In 11 (19 per cent) of the 58 cases of adenomatous goiter without hyperthyroidism intra-adenomatous parenchymatous hypertrophy was graded 1. In no case was the parenchymatous hypertrophy found to be greater than grade 1. Thus in 81 per cent of the nontoxic adenomas minimal or no columnar epithelium was present.

Relationship of Basal Metabolic Rate to Intra-Adenomatous Hypertrophy: Data from Surgical Series

Basal Metabolic Rate, Percentage	Total Cases	Intra-Adenomatous Hypertrophy				
		None Present (Grade 0)	Grade			Present; Percentage of Total
			One	Two	Three	
−20 to −10	14	11	3	..	..	21
− 9 to 0	26	22	4	..	..	15
+ 1 to +10	18	14	4	..	..	22
+11 to +20	19	12	4	3	..	37
+21 to +30	36	24	10	1	1	33
+31 to +40	39	26	8	3	2	33
+41 to +50	10	5	3	2	..	50
+51 to +60	8	2	4	2	..	75
+61 to +70	1	1	..	..	..	0
+71 to +80	1	1	..	..	..	0
+81 to +90	0	..	..	..	..	..
+91 to +100	1	1	..	..	..	0

In 43 (37 per cent) of the 115 adenomas with hyperthyroidism, intra-adenomatous parenchymatous hypertrophy was found. In 29 cases (25 per cent) the intra-adenomatous parenchymatous hypertrophy was grade 1, in 11 cases (10 per cent) it was grade 2 and in 3 cases (3 per cent) it was grade 3. In no case was it graded 4. In 72 cases minimal or no columnar epithelium was found (table).

The table demonstrates that some correlation exists between the degree of hyperthyroidism and the presence of intra-adenomatous parenchymatous hypertrophy in this series in which the clinical diagnosis was adenoma of the thyroid gland with or without hyperthyroidism.

COMMENT AND SUMMARY

Tissue from 338 thyroid glands was studied. This consisted of tissue from 165 thyroid glands obtained at necropsy in a period of six months and of thyroid tissue removed at operation in 58 cases of

adenomatous goiter without hyperthyroidism and in 115 cases of adenomatous goiter with hyperthyroidism. It was required for inclusion in the study that the extra-adenomatous thyroid tissue in the surgically removed glands should not have the histologic picture of exophthalmic goiter, that is, parenchymatous hypertrophy of more than grade 1. This restriction on selection of cases made it reasonably certain that cases of adenomatous goiter with and without hyperthyroidism were studied in almost all instances. The adenomatous goiters in the surgical series were, on an average, much larger than those removed at necropsy, and the average age of the subjects was considerably less. The study of the necropsy material indicated that nodular thyroid tissue did not greatly increase the average weight of the thyroid gland unless the nodules were adenomas. The large thyroid nodules were usually adenomas. From the surgical series it would appear that the presence of hyperthyroidism does not greatly increase the average weight of adenomatous goiters and the size of the adenoma cannot be correlated with hyperthyroidism in this series.

The sex incidence of adenomatous goiter in this series is of interest. In the necropsy group 22 per cent of the men and 46 per cent of the women had adenomatous goiters. In the surgical series in this group of patients who had adenomatous goiter without hyperthyroidism 12 per cent were men and 88 per cent were women; in the group of patients with hyperthyroidism 20 per cent were men and 80 per cent women. However, the total number of patients included in the entire series is rather small for statistical analysis.

Analysis of the necropsy material revealed that 4 per cent of the adenomas contained malignant growths. This observation might be pertinent in indicating whether a small adenoma should be removed surgically.

In the study of the surgical material intra-adenomatous parenchymatous hypertrophy, grade 1, was encountered in approximately a fifth of the cases of adenomatous goiters without hyperthyroidism. In the other four fifths of the cases there was no intra-adenomatous parenchymatous hypertrophy.

In the adenomatous goiters with hyperthyroidism surgically removed, intra-adenomatous parenchymatous hypertrophy was present in nearly two fifths of the cases. In about a third of these the intra-adenomatous parenchymatous hypertrophy present was higher than grade 1.

In the surgical series some correlation was found to exist between the frequency of occurrence of intra-adenomatous parenchymatous hypertrophy and the degree of hyperthyroidism.

REGULATION OF LONGITUDINAL BONE GROWTH

STERLING G. PARKER, M.D.
DECATUR, ILL.

THE MECHANISM of control of individual stature has been a subject for extensive research and conjecture for two centuries or more, and yet it is little understood. Growth is an inherent property of living matter, but the regulation of growth is under more specific controls which can be altered by chemical or other means that disturb the normal physiologic balance of tissue metabolism. If we could fully understand these factors, then we should be able to govern skeletal growth, to some extent at least, of normal growing people and to alter the course of pathologic growth when it is produced by physiologic imbalances.

It is well known that many factors can stimulate, inhibit or halt longitudinal bone growth in a given bone or extremity, depending on the mechanism involved. In general, conditions which produce hyperemia, and hence increase metabolic activity of the part, produce an increased rate of longitudinal bone growth during the period that the hyperemia exists.[1] Processes which decrease local metabolism [2] or interfere with the normal influence of stress or strain [3] slow longitudinal skeletal growth of the involved extremity, and anything which destroys the epiphysial cartilage will, of course, halt growth at that epiphysis permanently. It is also well known that nutritional deficiencies can cause gross disturbances of growth, which are pathologic states only to be considered here as they may be related to an understanding of normal bone growth. Congenital and acquired disorders will likewise be described only when they are helpful in clarifying the mechanism of regulation of growth.

Dr. Parker was formerly a Fellow in Orthopaedic Surgery, Northwestern University Medical Specialty Training Program.

1. (*a*) Compere, E. L., and Adams, C. O.: Studies of Longitudinal Growth of Long Bones, J. Bone & Joint Surg. **19**:922, 1937. (*b*) Müsenbach, R. G.: A Consideration of the Chemical and Mechanical Stimulation of Bone with Reference to the Epiphyseal and Diaphyseal Lines: Results of Animal Experimentation, Am. J. Orthop. Surg. **8**:28, 1910.

2. Armstrong, W. D.: Bone Growth in Paralyzed Limbs, Proc. Soc. Exper. Biol. & Med. **61**:358, 1946.

3. Howell, J. A.: An Experimental Study of the Effect of Stress and Strain on Bone Development, Anat. Rec. **13**:233, 1917.

HISTORICAL OBSERVATION

Stephen Hales [4] in 1727 scientifically recorded his observations on bone growth and thus initiated a study which has since grown in scope and magnitude. Using a half-grown chick, he pierced two holes in its legs at a measured distance with a sharp-pointed iron and found that two months later the marks were still equidistant, although the leg had grown 1 inch (2.54 cm.) in length. He concluded that this growth in length was from the epiphysis and that proper nutritive matter was necessary for its growth. Duhamel [5] confirmed this in 1743 in the pigeon and in the dog. The classic experiments of John Hunter [6] showed more accurately that normal longitudinal growth of the shaft of a long bone occurred only at the epiphysis. Also, by using Belchier's observation [7] that animals fed on madder root had a red tinge to their bones, he showed that the increase in diameter of bone was due to new bone being formed on the exterior of the shaft. These conclusions have been confirmed by Compere,[1a] Müsenbach,[1b] Humphry,[8] Wegner,[9] Haas,[10] Gatewood and Mullen [11] Payton,[12] Selye,[13] Phemister,[14] Bisgard and Bisgard,[15] Siegling,[16] and Aries.[17] From

4. Hales, S.: Statical Essays, London, W. Innys [and others], 1727, vol. 1, p. 339.

5. Duhamel, H. L.: Cinquieme memoire sur les os, Mém. Acad. Roy. d. Sc., 1743, p. 111, cited by Humphry.[8]

6. Hunter, J.: Experiments and Observations on the Growth of Bones, from the Papers of the Late Mr. Hunter with Notes, edited by James F. Palmer, 1835, vol. 4, p. 315.

7. Belchier, J.: An Account of the Bones of Animals Being Changed to a Red Colour by Aliment Only, Phil. Tr., London **39**:287, 1736.

8. Humphry, G. M.: Observations on the Growth of Long Bones and of Stumps, Med.-Chir. Tr., London **44**:117, 1861.

9. Wegner, G.: Ueber das normale und pathologische Wachsthum der Röhrenknochen, Virchows Arch. f. path. Anat. **61**:44, 1874.

10. Haas, S. L.: Interstitial Growth in Growing Long Bones, Arch. Surg. **12**:887 (April) 1926.

11. Gatewood, M. D., and Mullen, B. P.: Experimental Observations on the Growth of Long Bones, Arch. Surg. **15**:215 (Aug.) 1927.

12. Payton, C. G.: The Growth in Length of the Long Bones in the Madder-Fed Pigs, J. Anat. **66**:414, 1932.

13. Selye, H.: On the Mechanism Controlling the Growth in Length of the Long Bones, J. Anat. **68**:289, 1934.

14. Phemister, D. B.: Bone Growth and Repair, Ann. Surg. **102**:261, 1935.

15. Bisgard, J. D., and Bisgard, M. E.: Longitudinal Growth of Long Bones, Arch. Surg. **31**:568 (Oct.) 1935.

16. Siegling, J. A.: Growth of the Epiphyses, J. Bone & Joint Surg. **23**:23, 1941.

17. Aries, L. J.: Experimental Analysis of the Growth Pattern and Rates of Appositional and Longitudinal Growth in the Rat Femur, Surg., Gynec. & Obst. **72**:679, 1941.

these studies it can be said positively that normal longitudinal growth of the shaft occurs only at the epiphysis. That this growth is from the diaphysial side of the epiphysis was further shown by Brücke,[18] who rotated the epiphysial cartilages in rabbits 180 degrees, demonstrating that bony apposition took place only on the side originally facing the diaphysis.

With the advent of the science of endocrinology, certain disturbances of skeletal growth were suspected of being associated with dysfunctions of the ductless glands, although Marie,[19] in a classic description of acromegaly in 1889, stated that the etiology of acromegaly was unknown but that certain cases could be attributed to syphilis. Massalongo [20] in 1892 attributed acromegaly to hyperfunction of the pituitary gland, and Furnivall [21] in 1898 collected 49 cases of acromegaly in all but 2 of which there were abnormalities of the pituitary gland at autopsy. Benda [22] in 1900 found that the element chiefly concerned in the hyperplasia of the pituitary was the eosinophilic cells, and Lewis [23] in 1905 found similar changes. Casseli [24] in 1900 was the first to note a suggestive retardation of development after hypophysectomy. This was shown conclusively by Crowe, Cushing and Homans in 1910 [25] and later by Aschnan [26] and Smith,[27] the latter also noting that there was atrophy of the thyroid and gonads as well as retardation of growth.

18. Brücke, F.: Zur Frage der Bedeutung des Epiphysenfugenknorpels für das Wachstum der langen Röhrenknochen, Virchows Arch. f. path. Anat. **279**:641, 1931.

19. Marie, P.: Acromegaly, Brain **12**:59, 1889.

20. Massalongo, R.: Sull' acromegalia, Riforma med. **8**:76 and 87, 1892.

21. Furnivall, P.: Pathological Report on a Case of Acromegaly, with the Analysis of the Results of Forty-Nine Post-Mortem Examinations on Cases of Acromegaly, J. Path. Soc., London **49**:204, 1898.

22. Benda, C.: Beiträge zur normalen und pathologischen Histologie der menschlichen Hypophysis cerebri, Klin. Wchnschr. **37**:1205, 1900.

23. Lewis, D. D.: Hyperplasia of the Chomophile Cells of the Hypophysis as the Cause of Acromegaly with Report of a Case, Bull. Johns Hopkins Hosp. **16**: 157, 1905.

24. Caselli, A.: Influenza della funziono dell' ipofisi sulla soiluppo dell' organisimo, nota preventiva sulla fisio-patologia della ghiandola pituitaria, Riv. sper di freniat., Reggio-Emilia, **176**:486, 1900.

25. Crowe, S. J.; Cushing, H., and Homans, J.: Experimental Hyphysectomy, Bull. Johns Hopkins Hosp. **21**:127, 1910.

26. Aschnan, B.: Pflüger's Arch. f. d. ges. Physiol. **146**:1, cited by Eaton, J. C.: The Influence of the Endocrines on the Skeleton, Glasgow M. J. **27**:93, 1946.

27. Smith, P. E.: Experimental Ablation of the Hypophysis in the Frog Embryo, Science **44**:280, 1916.

Early investigators,[28] in an attempt to identify a specific function of the pituitary gland, fed fresh tissue to animals without any effect except questionable retardation of growth. They also used alcoholic extracts, without any definite conclusions. In 1921 Evans and Long [29] prepared an alcoholic extract of fresh pituitary glands, which was injected into rats intraperitoneally. They noted a consistent increased rate of growth in the experimental animals. In the treated animals a mild degree of gigantism was produced; the rats grew to twice the size of controls. In these animals the skeleton was invariably larger and heavier. Later they showed that the substance was not effective when administered orally.[30] These experiments formed the basis for the identification of the pituitary gland as the organ occupying the highest position in the endocrine order of growth regulators.

The relationship of the thyroid gland to skeletal growth was noted early in the history of endocrinology. Von Eiselberg [31] obtained stunting in goats subsequent to removal of the thyroid gland in 1894, and Langhans [32] described the changes occurring in the cretin, noting the small, indistinct cells of the epiphysial cartilage. MacCallum [33] described in accurate detail the anatomy of the myxedematous idiot in whom aplasia of the thyroid, gonad infantilism and hypertrophy of the hypophysis were found. He concluded that it was a general nutritional disturbance secondary to the thyroid aplasia. That other glands were also related to skeletal growth was demonstrated by Poncet [34] and Sellheim,[35] who were the first to demonstrate experimentally the delay-

28. Aldrich, T. B.: On Feeding Young White Rats the Posterior and the Anterior Parts of the Pituitary Gland, Am. J. Physiol. **31**:94, 1912. Robertson, T. B.: The Influence of Tethelin, the Growth-Controlling Principle of the Anterior Lobe of the Pituitary Body, upon the Growth of the White Mouse, J. Biol. Chem. **24**:397, 1916. Robertson, T. B.: The Influence of the Anterior Lobe of the Pituitary Body upon the Growth of the White Mouse, ibid. **24**:385, 1916.

29. Evans, H. M., and Long, J. A.: The Effects of the Anterior Lobe Administered Intraperitoneally upon Growth, Maturity and Oestrous Cycles of the Rat, Anat. Rec. **21**:62, 1921.

30. Evans, H. M., and Long, J. A.: Characteristic Effects upon Growth, Oestrus and Ovulation Induced by the Intraperitoneal Administration of Fresh Anterior Hypophyseal Substance, Proc. Nat. Acad. Sc. **8**:38, 1922.

31. Von Eiselberg, A.: Arch. f. Klin. Chir. **49**:207, 1897.

32. Langhans, T.: Anatomische Beiträge zur Kenntniss der Cretinen, Arch. f. path. Anat. u. Physiol. **149**:155, 1897.

33. MacCallum, W. G., and Fabyan, M.: On the Anatomy of a Myxoedematous Idiot, Johns Hopkins Hosp. Bull. **18**:341, 1907.

34. Poncet, A.: De l'influence de la castration sur le developpement du squelette, recherches experimentales et cliniques, Compt. rend. Soc. de biol. **55**:65, 1903.

35. Sellheim, H.: Kastration und Knochenwachstum, Beitr. z. Geburtsh. u. Gynäk. **2**:236, 1899.

ing effect of castration on epiphysiodiaphysial union and noted that natural castration in human beings resulted in consistent increases in average skeletal height.

EFFECTS OF THE ANTERIOR LOBE OF THE PITUITARY ON BONE GROWTH

Removal of the Anterior Lobe.—In growing rats most investigators have found an immediate and complete cessation of growth after total hypophysectomy.[36] In puppies almost total cessation of growth is seen soon after total hypophysectomy,[37] but Reichert and Dandy [37a, b] showed that there was slight but definite skeletal growth after the removal of the pituitary for a period of two or three weeks in contrast to the immediate cessation of growth observed in rats. This could theoretically be explained by the presence of residual hormone. The epiphysial lines remained open in these puppies without evidence of closure long after closure had occurred in the controls. Another uniform finding after hypophysectomy has been the decrease in the appetite of the animal, but it is only recently that this has been accurately correlated with the changes in growth. Samuels [38] showed that hypophysectomized rats which were fed by stomach tube a diet sufficient to maintain growth in controls would continue to gain weight at a diminished rate. They would also continue to store small quantities of nitrogen and large quantities of fat, which indicates a marked disturbance in the intermediate metabolism. He also observed that there was a relatively uniform increase in the weight of the femurs and slow skeletal growth. The rate of gain was about 10 per cent of that of the controls. The uniformity of the increase indicated that it was probably not due to the presence of residual hormone during the first few days but was a basal growth level which could be maintained in the absence of pituitary hormones. That regeneration as well as growth is interfered with is shown by a failure of regenerative powers following hypophysectomy in the newt.[39]

36. (*a*) Smith, P.: The Disabilities Caused by Hypophysectomy and Their Repair, J. A. M. A. **88**:158 (Jan. 15) 1927. (*b*) Smith, P. E.: Hypophysectomy and a Replacement Therapy in the Rat, Am. J. Anat. **45**:205, 1930. (*c*) Freud, J.; Levie, L. H., and Kroon, D. B.: Observation on Growth (Chondrotrophic) Hormone and Localization of its Point of Attack, J. Endocrinol. **1**:56, 1939.

37. (*a*) Reichert, F. L.: The Results of Replacement Therapy in an Hypophysectomized Puppy, Endocrinology **12**:451, 1928. (*b*) Dandy, W. E., and Reichert, F. L.: Studies on Experimental Hypophysectomy in Dogs, Bull. Johns Hopkins Hosp. **62**:122, 1938. (*c*) Crowe and others.[25] (*d*) Aschnan.[26]

38. Samuels, L. T.; Reinecke, R. M., and Bauman, K. L.: Growth and Metabolism of Young Hypophysectomized Rats Fed by Stomach Tube, Endocrinology **33**:87, 1943.

39. Richardson, D.: Thyroid and Pituitary Hormones in Relation to Regeneration, J. Exper. Zool. **100**:417, 1945.

Histologically certain changes are observed constantly after hypophysectomy.[40] In the epiphysial line the cells in the zone of proliferation are small, with pyknotic nuclei, and are reduced in number. The cartilage columns are regular but narrower, with an increased amount of matrix between them. The cells of the vesicular zone appear shrunken and the lacunas small, and there is a narrowing of this zone. The erosion zone is inactive. In the diaphysis the disappearance of the trabeculae is striking, which is explained only by an actual absorption of bone without an actual increase in the number of osteoclasts. The marrow shows a tremendous increase in fat content at the expense of the myeloid elements. As a result of these changes there is then, about twenty-five days after hypophysectomy, a reduction in the width of the epiphysial line. The progressive, severe atrophy of both the primary and secondary spongiosa may be seen by the seventh to the thirteenth day.[41]

Accompanying the changes in skeletal growth there are also gross and microscopic changes in other organs.[42] All organs are normal with the exception of the thyroid and adrenal glands and the gonads. Grossly there is atrophy of the adrenal cortex, but microscopically there is no deviation from the normal. The testes or ovaries are atrophied and show all signs of immaturity. There is little glandular tissue in the breasts of the animals. The changes in the thyroid are constant. There is pronounced atrophy, with smaller acini and a diminished amount of colloid.[37b]

The great reduction in the growth of the skeleton and musculature in the presence of available foodstuffs would favor the view that there is a reduction in the ability to synthesize structural elements following hypophysectomy, but the fact that wounds heal readily in hypophysectomized animals [38] indicates that the process is not completely inhibited. The slow increase in carcass nitrogen and the gradual growth of some organs further support the hypothesis that the removal of the pituitary gland eliminates a factor which catalyzes the growth process but which is not essential for it. It is possible that the synthesis of proteins is catalyzed by pituitary hormones.

---

40. (*a*) Beck, H. M.; Simpson, M. E.; Marx, W., and Kibrick, E.: Bioassay of the Pituitary Growth Hormone, Endocrinology **32**:13, 1943. (*b*) Ray, R. D.; Evans, H. M., and Becks, H.: Effect of the Pituitary Growth Hormone on the Epiphyseal Disc of the Tibia of the Rat, Am. J. Path. **17**:509, 1941.

41. Ingalls, T. H., and Hayes, D. R.: Epiphyseal Growth: The Effect of Removal of the Adrenal and Pituitary Glands on the Epiphyses of Growing Rats, Endocrinology **29**:720, 1941.

42. Footnotes 27 and 36 *a*, *b*.

HYPOPITUITARY STATES AND RELATIONSHIP TO HEREDITARY DWARFISM

Retardation of growth is seen in human beings as well as in experimental animals in association with hypopituitarism. Simmonds [43] in 1916 described a 9 year old girl who died of conditions simulating the emaciation of tuberculosis and who at autopsy was found to have a basophilic tumor of the hypophysis that had destroyed the remainder of the gland substance, but Erdheim [44] was the first to recognize the hypophysial origin of a dwarflike stunting of growth which may occur with the early destruction of the hypophysis—in his case a teratoma. The skeleton in such cases remains like that of a child with open epiphysial lines, with atrophy of the thyroid, gonads and adrenal glands. The characteristic delay in development of the ossification centers is the prominent feature, the epiphyses remaining open beyond the usual time. This growth defect, combined with delayed and subnormal sexual maturation, normal intelligence and normal mental faculties, is typical of the hypopituitary dwarf.[45]

The growth pattern of clinical hypopituitarism corresponds, then, to that seen in experimental animals in that there is a certain amount of growth at a basal level, which will occur in the presence of adequate foodstuffs.

Hereditary dwarfism appears as a mutation in the mouse. Since these dwarfs are entirely sterile, they can be produced only by heterozygous parents or occasionally from one that has received pituitary replacement therapy. There are no eosinophils in the anterior pituitary in the dwarfs. The dwarfism is essentially a retarded skeletal time curve, since they will continue to grow after normal mice have ceased to grow.[46] These animals are not true hereditary dwarfs, the term being reserved for dwarfs that are normal in every respect except for their size.

True hereditary dwarfism in the human being occurs but is not a true pathologic condition, for neither the skeleton nor other organs show evidence of abnormality or disease except for their small size. Puberty occurs at the normal age, and sex function is normal. Growth is slow and far below average, and this applies to the differential growth

43. Simmonds, M.: Ueber Kachexie hypophysären Ursprungs, Deutsche med. Wchnschr. **42**:190, 1916.

44. Erdheim, J.: Pathologie der Hypophysengeschwulste, Ergebn. d. allg. Path. u. path. Anat. **21**(11):482, 1926.

45. (*a*) Gardiner-Hill, H.: Abnormalities of Growth and Development, Brit. M. J. **1**:1302, 1937. (*b*) Shelton, E. K.: The Clinical Aspects of Dwarfing, Endocrinology **30**:1000, 1942. (*c*) Grollman, A.: Essentials of Endocrinology, ed. 2, Philadelphia, J. B. Lippincott Company, 1947, p. 101.

46. Boettiger, E., and Osborn, C. M.: A Study of Natural Growth and Ossification in Hereditary Dwarf Mice, Endocrinology **22**:447, 1938.

of the skeleton as well. The racial form is typified by the pygmies of Central Africa and is essentially a hereditary characteristic and dependent on the genetic constitution.[47]

Although endocrine constitution is largely determined by heredity, work of experimental embryologists suggests that the endocrine influences are not the main cause of racial peculiarities. Harrison,[48] in experimental work on transplantation of limbs of salamanders, has shown that in the same endocrine environment limbs and other structures from two species of different sizes will maintain their own rate of growth and reach the ultimate size and form characteristic of the species. This work indicates that there is an inherited growth capacity which is influenced by, but not dependent on, the endocrine constitution of the individual.

EFFECT OF SUBSTITUTION THERAPY WITH EXTRACTS OF THE ANTERIOR HYPOPHYSIS ON NORMAL AND HYPOPITUITARY ANIMALS AND ON HUMAN BEINGS

After Evans' work,[29] in which alcoholic extracts of the anterior pituitary produced marked alterations of the growth pattern in experimental rats, a great deal of work has been done, some of which has led to conflicting conclusions. A pure substance from the anterior lobe of the pituitary which will produce an effect only on skeletal growth has not been chemically isolated and identified, and this partially accounts for so much divergence of opinion. A globular fraction has been separated from extracts of the anterior hypophysis which contains the growth-promoting principle.[49] From osmotic pressure determinations the molecular weight is 44,250, and experiments with electrophoresis show an isoelectric point at p_H 6.85. The hormone is more stable in alkaline solution and can be destroyed by pepsin and trypsin.[50] The effect on the epiphysis of this substance when administered to hypophysectomized rats is so uniform that this reaction has been used for its bioassay.[40a] The initial effect on the epiphysial cartilage is predominently chondrogenesis. Activation of osteogenesis follows later, after six to eight days, at which time the normal equilibrium between chondrogenesis and osteogenesis is established, with a return of the

47. Gardiner-Hill, H.: Abnormailities of Growth and Development, Brit. M. J. **1**:1241, 1937.

48. Harrison, R. G.: Heteroplastic Grafting in Embryology in Harvey Lectures, 1933-1934, Baltimore, Williams & Wilkins Company, 1935, p. 116.

49. Teel, H. M.: A Method for Purification of Extracts Containing the Growth Promoting Principle of the Anterior Hypophysis, Science **69**:405, 1929.

50. Li, C. H.; Evans, H. M., and Simpson, M. E.: Isolation and Properties of the Anterior Hypophyseal Growth Hormone, J. Biol. Chem. **159**:353, 1945.

youthful type of epiphysial cartilage.[51] This activation of osteogenic processes can be accomplished as long as one year or more after hypophysectomy in the rat,[52] and it can be accomplished when other known contaminating hormones are removed, as evidenced by the continued growth with no change in the atrophic thyroid, gonads or adrenal cortex.[53]

Replacement therapy using homeotransplants of the anterior pituitary in the rat restores the animals to normal, or nearly normal.[36a, b] Heterotransplants in puppies [37a] using the rabbit pituitary will stimulate the growth but not for a period sufficient for the animals to obtain normal size before closure of the epiphysial lines occurs.

Injection of anterior pituitary extract in normal growing rats causes a decided stimulation of endochondral ossification, with little disturbance of the equilibrium between the formation of cartilage and bone, and an overstimulation of normal periosteal bone growth.[54] This response is not changed by thyroparathyroidectomy.[55] In 6 month old rats which have reached a physiologic state of growth inactivity (the epiphyses do not close in the rat) there is growth response after the anterior lobe extracts are administered and histologic evidence of active growth in the epiphysial cartilage plates and in the adjacent spongiosa.[56] Similar stimulative effects are noted in the growing guinea pig and dog,[57]

---

51. (*a*) Marx, W.; Simpson, M. E., and Evans, H. M.: Specificity of the Epiphyseal Cartilage Test for the Pituitary Growth Hormone, Proc. Soc. Exper. Biol. & Med. **55**:250, 1944. (*b*) Becks, H.; Simpson, M. E.; Marx, W.; Li, C. H., and Evans, H. M.: Antagonism of Pituitary Adrenocorticotropic Hormone (ACTH) to Action of Growth Hormone on Osseous System of Hypophysectomized Rats, Endocrinology **34**:311, 1944. Freud and others.[36c] Ray and others.[40b]

52. Becks, H.; Simpson, M. E.; Evans, H. M.; Ray, R. D.; Li, C. H., and Asling, W.: Response to Pituitary Growth Hormone and Thyroxin of the Tibias of Hypophysectomized Rats after Long Post-Operative Intervals, Anat. Rec. **94**:631, 1946.

53. Smith, P. E.: Increased Skeletal Effects in Anterior Pituitary Growth Hormone Injections by Administration of Thyroid in Hypophysectomized, Thyroparathyroidectomized Rats, Proc. Soc. Exper. Biol. & Med. **30**:1252, 1933.

54. Handelsman, M. B., and Gordon, E. F.: Growth and Bone Changes in Rats Injected with Anterior Pituitary Extract, J. Pharmacol. & Exper. Therap. **38**:349, 1930. Ray, R. D.; Evans, H. M., and Becks, H.: The Effect of Growth Hormone Injections on the Costochondral Junction of the Rat Rib, Anat. Rec. **82**: 67, 1942. Ray and others.[40b]

55. Becks, H.; Kibrick, E. A., and Evans, H. M.: The Bone Histology of Adult Male Rats Thyro-Parathyroidectomized When One Month of Age, J. Exper. Zool. **89**:297, 1942.

56. Ross, E. S., and McLean, F. C.: The Influence of the Growth Promoting Hormone of the Anterior Lobe of the Pituitary upon Growth Activity in the Long Bones of the Rat, Endocrinology **27**:329, 1940.

57. Silberberg, M.: Effects of Extract of Cattle Anterior Pituitary Gland on Endochondral Ossification in Young Guinea Pigs, Proc. Exper. Biol. & Med. **32**:1423, 1935.

in which there is hypertrophy and hyperplasia of the growth cartilage, which is subsequently quickly calcified and replaced by bone. The epiphysial line, therefore, undergoes premature closure under the influence of the extract. Another instance of the acceleration of the tissue time curve by the administration of pituitary extracts is shown by the acceleration of the formation of cancellous bone occurring in the abdominal fascia around the urinary bladder transplants of young pigs.[58]

In dwarf mice, in which there is a hereditary absence of the eosinophilic cells in the anterior pituitary, with resultant retarded skeletal time curve, daily implantations of normal pituitaries will restore normal growth. Riddle and others [59] have been able to restore skeletal growth in these mice by using prolactin and thyrotropic hormones either separately or together, when there is a synergistic action. This has been the basis for their contention that the growth hormone is not an individual factor but that it is a summation of several stimulating actions through other endocrine glands.

Clinically the treatment of true pituitary dwarfism has been unsatisfactory apparently because there is no highly potent and purified preparation for clinical use.[60]

HYPERPITUITARISM

The strongest evidence in favor of a specific growth hormone being secreted by the hypophysis is the clinical occurrence of gigantism in the adolescent and of acromegaly in the adult in association with evidence of overactivity of the hypophysis. Experimentally a mild degree of gigantism in rats was produced by Evans and Long,[29] but this is not easily or consistently produced, and the degree of overgrowth is limited. Others [61] have produced a condition in dogs, by using anterior pituitary extract, simulating the acral enlargement observed in human acromegaly. Definite skeletal overgrowth with hyperostosis is seen in these animals at autopsy.

---

58. Silberberg, M.; Atherton, H. R., and Copher, G. H.: Effects of Bovine Anterior Hypophyseal Extract on Urinary Bladder Transplants in Young Dogs, Ann. Surg. **120**:680, 1944.

59. Bates, R. W.; Loanes, T., and Riddle, O.: Evidence from Dwarf Mice Against the Individuality of Growth Hormone, Proc. Soc. Exper. Biol. & Med. **33**:446, 1935.

60. (*a*) Finkler, R. S.; Furst, N. J., and Klein, M.: Clinical and Roentgenological Study of the Effects of Hormonal Therapy on Bone Growth, Radiology **43**:346, 1944. (*b*) McCullagh, E. P., and Rossmiller, H. R.: Methyl Testosterone —Effect upon Body Weight and Growth, J. Clin. Endocrinol. **1**:507, 1941. (*c*) Grollman.[45c]

61. Putnam, T. J.; Benedict, E. B., and Teel, H. M.: Experimental Canine Acromegaly Produced by Injection of Anterior Lobe Pituitary Extract, Arch. Surg. **18**:1708 (April) 1929. Teel, H. M., and Cushing, H.: Studies in the Physiological Properties of the Growth-Promoting Extracts of the Anterior Hypophysis, Endocrinology **14**:157, 1930.

True pituitary gigantism is rare because the eosinophilic adenoma of the anterior pituitary usually occurs in adult life.[47] When it does occur, it usually starts at the time of puberty. Acromegaly is almost always associated with an eosinophilic adenoma or hyperplasia of the acidophilic cells of the anterior hypophysis. This was demonstrated in all but 2 of the 100 cases analyzed by Bailey and Davidoff[62] and is generally accepted to be a constant finding. In gigantism the increased growth is symmetric, but it is usually followed by the asymmetric growth characteristic of acromegaly when the major epiphyses close, producing an acromegalic giant.

Just as true hereditary dwarfism is not a pathologic condition, true hereditary gigantism is not a pathologic condition. Neither the skeleton nor other organs show any evidence of abnormality or disease except for their size. It is a hereditary characteristic and dependent on the chromosomal rather than the endocrine constitution.[63]

HYPOTHYROIDISM AND ATHYROIDISM

As noted earlier, a relationship between skeletal growth and the activity of the thyroid gland was noted early in the history of endocrinology. Experimentally, young rats,[64] dogs and cats,[65] rabbits,[66] frogs,[67] monkeys,[68] sheep and goats[69] show considerable retardation

62. Bailey, P., and Davidoff, L. M.: Concerning the Microscopic Structure of the Hypophysis Cerebri in Acromegaly, Am. J. Path. **1**:185, 1925.

63. Gardiner-Hill.[47] Harrison.[48]

64. (*a*) Hammett, F. S.: The Effects of the Loss of the Thyroid and Parathyroid Glands at One Hundred Days of Age on the Growth in Body Length, Body Weight and Tail Length of Male and Female Albino Rats, Am. J. Physiol. **63**:218, 1922. (*b*) Salmon, T. N.: The Effect in the Growth Rate of Thyroparathyroidectomy in Newborn Rats and of the Subsequent Administration of Thyroid, Parathyroid and Anterior Hypophysis, Endocrinology **23**:446, 1938. (*c*) Becks, H.; Ray, R. D.; Simpson, M. E., and Evans, H. M.: Effect of Thyroxin and the Anterior Pituitary Growth Hormone on Endochondral Ossification, Arch. Path. **34**:334 (Aug.) 1942.

65. Dott, N. M., and Frazier, J.: The Influence of Experimental Pituitary and Thyroid Derangements upon the Developmental Growth of Bone, Abstract, communication to the Eleventh International Congress of Physiology, Edinburgh, 1923, p. 107.

66. Hunter, M. W., and Sawin, P. B.: The Effects of Thyroidectomy on the Skull of the Domestic Rabbit, Am. J. Anat. **71**:417, 1942.

67. Terry, G. S.: Effects of the Extirpation of the Thyroid Gland upon Ossification in Rana Pipiens, J. Exper. Zool. **24**:567, 1917-1918.

68. Fleischmann, W.; Shumacker, H. B., Jr.; Straus, W. L.: Influence of Age on the Effect of Thyroidectomy in the Rhesus Monkey, Endocrinology **32**: 238, 1943.

69. Goldberg, S. A., and Simpson, S.: Osseous and Muscular Changes in Thyroidectomized Sheep, Proc. Soc. Exper. Biol. & Med. **23**:132, 1926.

of growth as one of the manifestations of thyroidectomy. Similarly, a delay in the unfolding of the osseous framework in children in association with a hypothyroid state is a constant finding.[70] In fact, in the absence of other pathologic changes, the skeletal development in childhood has been regarded as a reliable index of the metabolic speed.[71]

Experimentally the degree of growth retardation varies with the species and with the age at which the hypothyroidism occurs. There is notable retardation in the appearance and development of the ossification centers, and, in prolonged thyroid deficiency, certain degenerative changes are noted in the cartilaginous epiphyses.[69] The epiphysial cartilages remain wide and infantile in appearance,[65] and histologically they show a lesser degree of calcification than normal and the proportion of matrix to cartilage cells is greater. There are depressed osteoblastic activity, inadequate capillary erosion, thick cartilaginous trabeculae and a marked increase of fat in the marrow.[72] This histologic picture, then, is not too unlike that seen after hypophysectomy.

In hypothyroidic infantilism in children, dwarfism is pronounced if the onset is early in life. Skeletal proportions are those of an infant, the head being large for the body and the limbs shorter in proportion to the trunk, with a resultant disproportionate skeleton. The ossification centers appear late, and when they do appear, they develop slowly. In the epiphysial center there may be multiple irregular islets of calcification, which may enlarge and coalesce to form an irregular, spongy, fluffy mass similar to that seen in osteochondritis.[73] The histologic changes in the epiphysial plate are similar to those seen in experimental hypothyroidism.[45a] While the skeletal changes are not too different from those in pituitary dwarfism, the similarity ends there, as the mental retardation and physical appearance make the thyroid dwarf strikingly different from the pituitary dwarf. Hypothyroid dwarfs also show a much greater degree of osseous retardation than pituitary dwarfs of the same chronologic age.[45b]

---

70. (*a*) Dorff, G. B.: Masked Hypothyroidism in Children, J. Pediat. **6**:789, 1935. (*b*) Shelton, E. K.; Lager, B. N., and Hoyt, E.: Cretinism, Endocrinology **27**:425, 1940. (*c*) Gardiner-Hill.[45a] (*d*) Shelton.[45b]

71. Shelton, E. K.: Osseous Development as an Index of Metabolic Speed, Endocrinology **17**:667, 1937.

72. Becks and others.[64c] Dott and Frazier.[65] Goldberg and Simpson.[69]

73. Lāwen, A.: Zur Kenntnis, der Wachstumsstörungen am Kretinenskelett, Deutsche Ztschr. f. Chir. **101**:454, 1909. Reilly, W. A.: Cretinoid Epiphyseal Dysgenesis, J. Pediat. **11**:786, 1937. Wilkins, L.: Epiphysial Dysgenesis Associated with Hypothyroidism, Am. J. Dis. Child. **61**:13 (Jan.) 1941. Brailsford, J. F.: The Radiology of Bones and Joints, ed. 3, Baltimore, Williams & Wilkins Company, 1945, p. 134.

In addition to the skeletal changes following hypothyroidism, pronounced structural changes in the pituitary have been observed.[74] There is an increase in the size and weight of the gland, reduction in the number of acidophils and an increase in the number of basophils, many of which are distended with a hyaline material. The gonads and secondary sexual organs are small and atrophic. The parathyroids, thymus and adrenals are normal.[75]

Replacement therapy in cretinic dwarfs results in a constant response. The first year there is usually 600 to 900 per cent of the previous annual increment, in the second year there is 25 to 50 per cent of the previous annual increment and in the third year growth will proceed at about the normal rate, but the expected normal skeletal development for the individual will not be achieved.[76] There is no adequate explanation for the initial spurt of growth in these dwarfs when they are given thyroid therapy. A normal growth curve can be obtained experimentally by continued administration of thyroid after thyroidectomy,[64b] and the normal histologic picture in the pituitary is maintained or, if a previous deficiency existed, restored.[74c]

HYPERTHYROIDISM

Hyperfunction of the thyroid gland in young persons produces a striking increase in the rate of development and of growth of the skeletal system, with advancement in the apparent age of the ossification centers being a constant roentgenologic finding.[77] Beilby [78] reported a case in which the onset of hyperthyroidism occurred before 1 year of age. At the chronologic age of 4 the skeletal age was that of a 9 year old child. While there is definite stimulation in the rate of growth, it is not enhanced as much as the skeletal aging, so that the final total growth may be less than would be expected. Because of this, gigantism is not produced by hyperthyroidism.

---

74. (*a*) Severinghaus, A. E.; Smelser, G. K., and Clark, H. M.: Anterior Pituitary Changes in Adult Male Rat Following Thyroidectomy, Proc. Soc. Exper. Biol. & Med. **31**:1127, 1934. (*b*) Liddell, H. S.: The Growth of the Head in Thyroidectomized Sheep, Anat. Rec. **30**:327, 1925. (*c*) Zeckwer, I. T.: Differences Between Castration Cells and Thyroidectomy Cells of the Pituitary of the Rat in Response to the Administration of Estrone and Thyroid Extract, Am. J. Path. **14**:773, 1938.

75. Moore, R. A.: A Textbook of Pathology, Baltimore, W. B. Saunders Company, 1944, p. 1059.

76. Shelton.[45b] Shelton and others.[70b]

77. Welti, H.: Maladie de Basedow chez l'enfant, Tr. Third Internat. Goiter Conf. & Am. A. Study Goiter, 1938, p. 101; cited by Black, J. B., and Webster, B.: Hyperthyroidism in Adolescent: Analysis of Eighteen Cases Under Eighteen Years of Age, J. Clin. Endocrinology **1**:861, 1941.

78. Beilby, G. E., and McClintock, J. C.: Hyperthyroidism in Children, New York State J. Med. **37**:563, 1937.

In mice [79] and rats,[80] experimental hyperthyroidism accelerates and intensifies the age changes of the skeleton. Thyroxin accelerates the conversion of the proliferating cartilage cells into cartilage cells of the hypertrophic type. It accelerates and increases the resorptive processes in the osseous tissues, leading to a complete epiphysiodiaphysial union at a premature age. Thyroid feeding in rats is followed by structural changes in the pituitary. The basophils are of maximum size and markedly increased in number. The acidophils are larger and stain more brilliantly [81]; however, no consistent changes are found in the anterior lobe of the pituitary in the human being in association with exophthalmic goiter.[82]

RELATIONSHIP OF THE THYROID AND THE PITUITARY

The interdependence of the pituitary gland and the thyroid gland for normal activity is exhibited by several different reactions. The atrophy of the thyroid in hypopituitary states and the hyperplasia in hyperpituitarism were discussed previously, as was the decreased number of eosinophilic cells in the anterior pituitary in hypothyroidism. Experimentally it was noted that there was hyperplasia of the eosinophilic cells in rats in hyperthyroidism, but this finding has not been apparent in human beings.

The thyroid response has been shown to be a result of the influence of the thyrotropic principle and not of the growth-promoting extracts,[82b] which exert their influence independently of the thyroid as demonstrated by the growth response to anterior pituitary extracts in thyroidectomized rats [83] and by the failure of growth in hypophysectomized animals treated with thyroid.[84] It has been suggested [85] that

79. Silberberg, M., and Silberberg, R.: Changes in the Skeletal Tissues of Mice Following the Administration of Thyroxin, Growth **4**:305, 1940.

80. Smith, E. E., and McLean, F. C.: Effect of Hyperthyroidism upon Growth and Chemical Composition of Bone, Endocrinology **23**:546, 1938. Becks and others.[64c]

81. Severinghaus, A. E.; Smelser, G. K., and Clark, H. M.: Anterior Pituitary Changes in Adult Male Rats Following Thyroxin Injections or Thyroid Feeding, Proc. Exper. Biol. & Med. **31**:1125, 1934.

82. (*a*) Wegelin, C.: L'hypophyse dans la maladie de Basedow, Ann. D'anat. Path., **15**:703, 1938, cited by Grollman, A.: Essentials of Endocrinology, Philadelphia, J. B. Lippincott Company, 1947, p. 217. (*b*) Cope, C. L.: The Anterior Pituitary Lobe in Graves' Disease and in Myxoedema, Quart. J. Med. **7**:151, 1938.

83. Silberberg, M., and Silberberg, R.: Effect of Acid Extract of Cattle Anterior Pituitary on Bone Repair in Thyroidectomized Guinea Pigs, Proc. Soc. Exper. Biol. & Med. **34**:108, 1936.

84. (*a*) Evans, H. M.; Simpson, M. E.; Pencharz, R. I.: Relation Between the Growth Promoting Effects of the Pituitary and the Thyroid Hormone, Endocrinology **25**:175, 1939. (*b*) Smith.[84a]

85. Evans, H. M.: Clinical Manifestations of Dysfunction of the Anterior Pituitary, J. A. M. A. **104**:465 (Feb. 9) 1935.

thyroid dwarfism is directly caused by inadequate pituitary function secondary to thyroid subnormality. If so, then the restoration of growth could be accomplished by the administration of either thyroid or pituitary extracts. This has been partially accomplished experimentally in rats,[84a] but clinical use of pituitary extracts in persons with hypothyroidism has been disappointing [86] in that no significant response has been found. This may be due to the lack of potency of the extract, but more probably the action of the thyroid hormone on growth is a phase of its action on metabolism and is less specific and essentially different from that of the anterior pituitary.

It is true, however, that the two hormones have a synergistic action when administered to normal rats,[84a] to thyroidectomized rats,[84c] to hypophysectomized and thyroidectomized rats [53] or to hypophysectomized rats.[52]

From the evidence available, it would seem that the capacity for growth is more dependent on the action of the pituitary and the intensity of growth is more dependent on the action of the thyroid hormone.

HYPOGONADISM

The effects of castration and of hypogonadism from other causes on skeletal growth in animals and human beings may be observed in ordinary life. Castration is a common practice, and it is well known that in animals castrated during the growth period longer limbs develop and that in the eunuch the extremities are longer in comparison with the trunk. It is also readily seen that true gigantism does not occur, and hence it is apparent that the sex hormones are not fundamentally necessary for the cessation of skeletal growth but only influence it. With these indisputable facts at hand, it would seem necessary to determine only the manner and degree in which the gonads influence growth; however, conflicting reports have been published on the effects of castration on growth.[87] Experimentally, most workers report a depression of growth following castration. There is a delay in the development of the epiphysial cartilages, followed by a reduction in the rate of pro-

86. Beard, E. E.: Cretinism, J. Clin. Endocrinol. **1**:293, 1941. Finkler and others.[60a] Shelton and others.[70b]

87. Pomerat, G. R., and Coe, R. C.: Bone Growth in the Long Term Castrate Albino Rat, Endocrinology **29**:1015, 1941. Rubinstein, H. S.; Abarbanel, A. R., and Kurland, A. A.: The Effect of Castration on Body Weight and Length of the Male Albino Rat, Endocrinology **25**:397, 1939. Tang, Y. Z.: Sex Difference in Growth in Gonadectomized Albino Rats, Anat. Rec. **80**:13, 1941. Silberberg, M., and Silberberg, R.: Effects of Ovariectomy and Long Continued Administration of APE of Cattle on Skeletal Tissues of Immature Guinea Pigs, Am. J. Path. **16**:505, 1940. Becks and others.[52]

liferation at the epiphysis, which represents the direct cause of the temporary reduction in body length seen in castrated animals. The epiphyses, however, remain open beyond the normal time, accounting for the mild disproportionate gigantism seen, with the extremities unduly long in comparison to the trunk.

After castration there are rather constant cellular reactions in the hypophysis. In rats, there is a decrease in the size and number of the acidophils and an increase in the number and size of basophils, some of which become vacuolated and assume a "signet ring" appearance and are known as "castration cells." [74c] At the same time, there is an increase in the gland's content of gonadotropic principles, probably due to the absence of an "inhibitor" substance of the gonads.[88] This increase in gonadotropic substance is probably associated with the changes in the basophilic cells, the changes in the eosinophilic elements representing the depressed growth.

HYPERGONADISM

Hypergonadism in the human being is found either with precocious development of the gonads, secondary to adrenal cortical tumors,[89] with certain tumors of the testicles or ovaries or in association with hypothalmic lesions which presumably stimulate the production of gonadotropic substance in the anterior pituitary.[90]

In animals, however, experimental hypergonadism can be produced by the injection of sex hormones and related compounds.

Hypergonadism results in a marked acceleration of growth and speed of skeletal maturation. Rowlands [91] reported a 9 year old boy, normal at the age of 6, who had an interstitial cell tumor of the testis and who grew to 5 feet (152 cm.) in a period of three years. Krabbe,[92] studying roentgenograms of epiphyses of children with precocious puberty, found the skeletal age well in adavnce of the chronologic age and reported a case in which a girl was 54 inches (137 cm.) tall at 7 years of age. The final growth is less than would be normally expected, which indicates that skeletal maturation is advanced more rapidly than

88. Best, C. H., and Taylor, M.: The Physiological Basis of Medical Practice, Baltimore, Williams & Wilkins Company, 1943, p. 1270.

89. Bergmann, B.: Sex Precocity and the Adrenogenital Syndrome, J. Pediat. **31**:142, 1947.

90. Gross, R. E.: Neoplasms Producing Endocrine Disturbances, Am. J. Dis. Child. **59**:579 (March) 1940.

91. Rowlands, R. P., and Nicholson, G. W.: Growth of the Left Testicle with Precocious Sexual and Bodily Development (Macro-Genito-Somia), Guy's Hosp. Rep. **99**:401, 1929.

92. Krabbe, K. H.: Early Synostosis of the Epiphyses with Dwarfism in Pubertas Precox, Endocrinology **3**:459, 1919.

skeletal growth. These studies also indicate that a sex hormone is related to the cessation of skeletal growth following puberty.

The use of estrogen, estrogenic substances and testosterone experimentally accelerates and intensifies the processes of skeletal aging and inhibits the proliferation of cartilage.[93] Daily injections of testosterone or estrogenic substances in castrated rats do not cause a change in the serum calcium or phosphorus, or in the fecal excretion of these elements,[94] or of the blood alkaline phosphatase.

With advancing age the following epiphysial changes occur. There is a decrease in proliferation of cartilage cells and a decrease in the conversion of resting cartilage cells to hypertrophic cartilage cells. There is an increase in the amount of chondromucoid substance and an increase in sclerosis, hyalinization and calcification of the cartilaginous matrix. There is a continuous absorption and solution of the newly formed metaphysial bone and finally of the nonproliferating epiphysial disk, leading to epiphysiodiaphysial union.[93c]

Injection of testosterone propionate in mice [95] and rats [96] promoted the aging of the epiphysial cartilages by inhibiting proliferative processes and promoting degeneration, hyalinization, sclerosis and calcification in the cartilage except when only small doses were administered,[97] in which instance significant stimulation of growth was noted without significant advance in skeletal age. In castrated mice only small doses are required to restore development of growth and development of the epiphysial cartilage,[95a] and hence this state probably more nearly approximates the normal. In rats the hypophysial changes following castration

93. (*a*) Silberberg, M., and Silberberg, R.: Response of Cartilage and Bone of Growing Mice to Testosterone Propionate, Arch. Path. **32**:85 (July) 1941; (*b*) Further Investigations Concerning the Influence of Estrogen on Skeletal Tissues, Am. J. Anat. **69**:295, 1941; (*c*) Effects of Hormones on the Skeleton of Mice, Guinea Pigs and Rats, Endocrinology **29**:475, 1941.

94. Buchwald, K. W., and Hudson, L.: The Biochemical Effects of Injections of Sex Hormones into Castrated Rats, Endocrinology **37**:301, 1945.

95. (*a*) Silberberg, M., and Silberberg, R.: Further Investigations on the Effect of the Male Sex Hormone on Endochrondral Ossification, Anat. Rec. **95**:97, 1946; (*b*) footnote [93a].

96. Rubinstein, H. S., and Solomon, M. L.: The Growth Depressing Effect of Large Doses of Testosterone Propionate in the Castrate Albino Rat, Endocrinology **28**:112, 1941.

97. Rubinstein, H. S.: Growth-Stimulating Effect of Testosterone Propionate, Proc. Soc. Exper. Biol. & Med. **44**:442, 1940. Rubinstein, H. S., and Solomon, M. L.: The Growth Stimulating Effect of Small Doses of Testosterone Propionate in the Castrate Albino Rat, Endocrinology **28**:229, 1941.

can be prevented by administration of testosterone.[98] Some workers [99] have failed to demonstrate any effect on skeletal growth by the use of testosterone, but for the most part these findings are accepted.

The use of testosterone as therapy for persons with hypogonadism has met with some success. There is a definite stimulation in the growth rate,[100] and if large doses are administered, significant advancement of the skeletal age over the chronologic age can be accomplished.[101] Weight cannot be used as a guide of growth because steroids, particularly those of the adrenal cortex, cause increase in weight for a while, owing to retention of sodium chloride and water.[60b]

As previously stated, injections of estrogen also accelerate skeletal aging in growing animals and when used over long periods, will cause significant retardation of growth in rats,[102] mice and guinea pigs.[98b] It inhibits the proliferation of cartilage and induces sclerosis of the cartilaginous matrix. On the other hand, estrogen inhibits processes of differentiation in the epiphysial cartilage and counteracts the solution processes which normally lead to the removal of the subepiphysial trabeculae and initiate epiphysiodiaphysial union. At the same time, there is a definite osteosclerosis by endosteal appositional growth.[103] Since this does not reflect longitudinal growth, it is probably an attempt

98. Wolfe, J. M., and Hamilton, J. B.: Response of Anterior Pituitary of Immature Castrated Rat to Testosterone and Related Compounds, Proc. Soc. Exper. Biol. & Med. **36**:307, 1937.

99. McEuen, C. S.; Selye, H., and Collip, J. B.: Effect of Testosterone on Somatic Growth, Proc. Soc. Exper. Biol. & Med. **36**:390, 1937. Turner, H. H.; Lachmann, E., and Hellbaum, A. A.: Effect of Testosterone Propionate on Bone Growth and Skeletal Maturation of Normal and Castrated Male Rats, Endocrinology **29**:425, 1941.

100. Webster, B., and Hoskins, W.: Influence of Androgen Therapy on Growth Rate of Hypogonadal Adolescent Boys, Proc. Soc. Exper. Biol. & Med. **45**:72, 1940.

101. McCullagh, E. P., and McGurl, F. J.: The Effect of Testosterone Propionate on Epiphyseal Closure, Sodium and Chloride Balance and a Sperm Count, Endocrinology **26**:377, 1940.

102. (*a*) Koenig, V. L.; Gassner, F. X., and Gustavson, R. G.: Effect of Estrone and Diethystilbestrol on Growth Rate of Rats and on Iodine Content of Thyroid, Am. J. Physiol. **144**:363, 1945. (*b*) Gaarenstroom, J. H., and Levie, L. H.: Disturbance of Growth by Diethylstilbestrol and Oestrone, J. Endocrinol. **1**:420, 1939. (*c*) Spencer, J.; Gustavson, R. G., and d'Amour, F. E.: Effect of Estrin Injections on the Growth Curve of Young Rats, Proc. Soc. Exper. Biol. & Med. **28**:500, 1931. Talbot, N. B.: The Effect of Estrogen on the Skeletal Age of Immature Rats, Endocrinology **25**:325, 1939.

103. Sutro, C. J.: Effects of Subcutaneous Injection of Estrogen upon Skeleton in Immature Mice, Proc. Soc. Exper. Biol. & Med. **44**:151, 1940. Bauer, W., and Rub, J. C.: Studies of Calcium and Phosphorus Metabolism: XVI. The Influence of the Pituitary Gland, J. Clin. Investigation **20**:295, 1940.

to store calcium, so it is compatible that there would be stimulation of endosteal appositional growth with resultant osteosclerosis and yet be decreased epiphysial and periosteal bone growth.

In addition to these effects, estrogen injected produces effects on other endocrine glands. There is hypertrophy of the adrenal cortex and of the pituitary.[104] In the latter there is degranulation of many or all of the basophils, which indicates that these cells are the source of gonadotropic hormone, and if large doses are used there is also degranulation of the acidophilic elements corresponding with the decreased growth.[105]

Synthetic estrogens will produce the same effects on growth as natural estrogens,[106] the only difference being that administration of growth hormone does not counteract the action of synthetic estrogen.[102b]

ACTION AND RELATIONSHIP OF SEX HORMONES TO THE GROWTH HORMONE

Estrogen and growth hormone both accelerate skeletal aging in growing animals, but they accomplish this effect in different ways. The pituitary growth principle stimulates growth and hastens epiphyseodiaphysial union by inducing premature regression and resorption of the epiphysial cartilage; estrogen, on the other hand, inhibits growth and resorption, thus delaying epiphysiodiaphysial union. The skeletal effects of estrogen can be modified by the administration of growth hormone; the two hormones oppose each other in their action on the growth of cartilage, but they cooperate in accelerating the age changes in the cartilage and in the overproduction of bone growth hormone by stimulating osteoblastic bone formation and estrogen by promoting hyalinization of the marrow and by inhibiting the resorption of bone. The two hormones thus do not neutralize each other, but each tends to exert its own effect on the receptor tissue.[107] The effects of estrogen are direct and not mediated by the action of the anterior lobe of the hypophysis. The hypophysial changes thus observed in hypergonadism and hypogonadism are secondary manifestations.

---

104. Korenchevsky, V., and Dennison, M.: Effect of Oestrone on Normal and Castrated Male Rats, Biochem. J. **28**:1474, 1934.

105. Wolfe, J. M., and Chadwich, C. S.: Quantitative Studies on the Structural Changes Induced in the Anterior Hypophysis by Injections of Oestrin, Endocrinology **20**:503, 1936. Wolfe and Hamilton.[98]

106. Noble, R. L.: Effect of Synthetic Oestrogenic Substance on the Body Growth and Endocrine Organs of the Rat, Lancet **2**:192, 1938. Koenig and others.[102a]

107. Silberberg, M., and Silberberg, R.: Combined Effects of an Estrogen and an APE on the Skeleton of the Growing Mouse, Arch. Path. **39**:381 (April) 1945.

Since the two hormones modify each other's effect to some extent, clinical use has been made of them. The use of ovarian extracts and testosterone has been moderately successful in arresting potential gigantism.[108]

RELATIONSHIP OF THE ADRENAL CORTEX TO BONE GROWTH

The relationship of the adrenal cortex hormone[109] to bone growth is less understood than that of the other endocrine substances. In adrenalectomized rats atrophy of the bone similar to that seen after hypophysectomy develops in five to eight days, which has led some[41] to believe that the organ is as essential for continued epiphysial growth as the pituitary and that both disturbances might have a common origin in the cessation of function of the adrenal cortex, since atrophy of the adrenal cortex is an inevitable sequence of hypophysectomy; however, these changes can be prevented in adrenalectomized animals by the administration of sodium chloride.[110]

By the administration of adrenal cortex hormone, crystalline derivatives of the hormone[111] or the adrenocorticotropic principle of the pituitary to normal rats[112] and to castrated rats,[113] almost complete inhibition of somatic growth can be obtained. There is a retardation in both chondrogenesis and osteogenesis, but the reduction in the width of the epiphysial cartilage is not so extreme as that following hypophysectomy. Also, in hypophysectomized animals osteogenesis ceases, whereas in rats treated with adrenocorticotropic hormone it continues

---

108. Currier, F. P.; Frantz, C. H., and Vander Meer, R.: Reduction of Growth Rate in Gigantism Treated with Testosterone Propionate, J. A. M. A. **117**:515 (Aug. 16) 1941. Fancher, J. K.: Some Observations on Anterior Lobe Hyperpituitarism, Endocrinology **16**:611, 1932. Goldzieher, M.: Growth and Sex Hormones, J. Clin. Endocrinol. **1**:924, 1941.

109. Hartman, F. A., and Thorn, G. W.: A Biological Method for the Assay of Cortin, Proc. Soc. Exper. Biol. & Med. **28**:94, 1930. Hartman, F. A.; Brownell, K. A.; Hartman, W. E.; Dean, G. A., and MacArthur, C. C.: The Hormone of the Adrenal Cortex, Am. J. Physiol. **86**:353, 1928.

110. Simpson, M. E.; Marx, W.; Becks, H., and Evans, H. M.: Response of Adrenalectomized Hypophysectomized Rats to the Pituitary Growth Hormone, Endocrinology **35**:234, 1944.

111. Wells, B. B., and Kendall, E. C.: The Influence of Corticosterone and C17 Hydroxydehydrococorticosterone (Compound E) on Somatic Growth, Proc. Mayo Clin., Staff Meet. **15**:324, 1940.

112. Ingle, D. J.; Higgins, G. M., and Kendall, E. C.: Atrophy of the Adrenal Cortex in the Rat Produced by Administration of Large Amounts of Cortin, Anat. Rec. **71**:363, 1938.

113. Moon, H. D.: Inhibition of Somatic Growth in Castrate Rats with Pituitary Extracts, Proc. Soc. Exper. Biol. & Med. **37**:34, 1937.

at a reduced rate.[114] In hypophysectomized animals, the stimulating effect of the administration of growth hormone can be almost completely nullified by the simultaneous use of adrenocorticotropic hormone.[115] If the animal is adrenalectomized, the adrenocorticotropic hormone has no effect, as would be expected.[116] Adrenocorticotropic hormone has no significant effect when administered alone to hypophysectomized animals.[51a] Animals which are both adrenalectomized and hypophysectomized show no more sensitivity to growth hormone when sodium chloride is given than do hypophysectomized animals.[117]

Clinically, excess secretion of the adrenals due to hyperplasia or neoplasm produces a marked advancement in growth and in skeletal age, but the advancement in skeletal age is greater in proportion than the spurt in growth.[118] Advancements of skeletal age from two to four years is not uncommon. There is an appreciable increase of androgens in the urine. While normally the steroids produced by the adrenal cortex are not androgenic, under pathologic influences androgenic steroids are produced.[89]

Usually the adrenal cortex probably has no relation to bone growth except as it is necessary for normal metabolism, but, in cases of tumor and other conditions producing hyperfunction certain steroids are excreted which produce the same effect as the sex hormones.

INDUCTION OF BONE GROWTH

From the evidence available, it is apparent that the thyroid, the gonads and the pituitary gland are intimately related to bone growth and to each other but that their function is more closely related to general tissue metabolism. Therefore, the question of their specificity is still debatable. The evidence indicates that their action is not specific but that their presence is essential for normal osseous growth. The decisive factor appears to be the "growth competence" of the tissue while the hormones act as growth organizers, the pituitary

114. Becks, H.; Simpson, M. E.; Li, C. H., and Evans, H. M.: Effects of Adrenocorticotropic Hormone (ACTH) on the Osseous System in Normal Rats, Endocrinology **34**:305, 1944.

115. Marx, W.; Simpson, M. E.; Li, C. H., and Evans, H. M.: Antagonism of Pituitary Adrenocorticotropic Hormone to Growth Hormone in Hypophysectomized Rats, Endocrinology **33**:102, 1943. Becks and others.[51b]

116. Evans, H. M.; Simpson, M. E., and Li, C. H.: Inhibiting Effect of Adrenocorticotropic Hormone on the Growth of Male Rats, Endocrinology **33**: 237, 1943. Becks and others.[114]

117. Simpson, M. E.; Marx, W.; Becks, H., and Evans, H. M.: Effect of Testosterone Propionate on the Body Weight and Skeletal System of Hypophysectomized Rats, Endocrinology **35**:309, 1944.

118. Kennedy, R. L. J.: Precocious Skeletal Development, J. A. M. A. **127**: 580 (March 10) 1945. Shelton.[45b] Gross.[90]

occupying the highest position. Furthermore, these hormones may act through an intermediary substance. Levander,[119] Lacroix[120] and Bertelsen[121] have been able to prepare an alcoholic extract of bone the fatty acid fraction of which when injected into muscular tissue produces cartilage and bone. Osteogenesis appears to occur by metaplasia of the surrounding conective tissue, the extract acting as a growth inductor. Blum,[122] in preparing phosphatase from long bones, found that the extract would produce ectopic bone when injected into muscles. Whether any relationship exists between these osteogenic substances and the hormones affecting bone growth remains to be seen.

SUMMARY

The longitudinal growth of long bones is primarily dependent on an inherited growth capacity and secondarily dependent on the endocrine constitution of the individual.

The secretions of the anterior lobe of the pituitary, the thyroid and the gonads are environmental factors in normal growth, and the secretions of the adrenal cortex may be under certain pathologic stimuli; of these, the anterior lobe of the pituitary occupies the highest order of the endocrine system.

The secretions of the anterior lobe of the pituitary, of the thyroid and of the gonads all accelerate and intensify the process of skeletal aging but accomplish this by each exerting its own effect on the receptor tissue.

These three organs are dependent on each other for their normal function.

A specific factor of the anterior pituitary is responsible for the maintenance of normal growth; however, a basal level of growth can be accomplished in its absence.

Thyroxin, by its action on metabolism, is primarily concerned with the intensity of growth.

Androgenic and estrogenic substances aid in the cessation of normal growth but are not essential for its occurrence.

---

119. Levander, G.: A Study of Bone Regeneration, Surg., Gynec. & Obst. **67**:705, 1938. Levander, G.: Tissue Induction, Nature, London **155**:148, 1945. Levander, G.: Alcohol-Soluble Osteogenetic Substance from Bone Marrow, Nature, London **157**:587, 1946.

120. Lacroix, P.: Recent Investigations on the Growth of Bone, Nature, London **156**:576, 1945; On the Origin of the Diaphysis, Anat. Rec. **92**:435, 1945; Organizers and the Growth of Bone, J. Bone & Joint Surg. **29**:292, 1947.

121. Bertelsen, A.: Experimental Investigations into Post-Foetal Osteogenesis, Acta. orthop. Scandinav. **15**:139, 1944.

122. Blum, G.: Phosphatase and the Repair of Fractures, Lancet **2**:75, 1944.

LIGATION OF THE VENA CAVA IN EXTENDING THROMBOPHLEBITIS

EUGENE E. CLIFFTON, M.D.*
NEW HAVEN, CONN.
AND
CAPTAIN J. C. NEEL
Medical Corps, Army of the United States

THE TREATMENT of venous thrombosis has been revolutionized in the past two decades by the use of anticoagulant drugs (heparin sodium and dicumarol®) and by ligation of the involved veins (usually the femoral vein). Ligation of the inferior vena cava has been carried out infrequently. It is evident that in the past few years interest in, and a study of, this formerly rare procedure have been greatly accelerated. Doubtless, the motivating force behind this increased interest is the usefulness of ligation as an additional weapon in our armamentarium to forestall the sudden catastrophe of embolic disease. The use of this measure is not advocated as a replacement for anticoagulant therapy or for ligation of the femoral vein, but rather as an additional method for use when these procedures may be inadequate; we feel that ligation of the vena cava is indicated much more frequently than it is used. After a careful review of the available literature and after general consideration, we question whether it should not replace ligation of the iliac veins, especially the left one.

We wish to describe a group of symptoms and signs which we have not found described elsewhere and which we believe indicate involvement of the lumbar veins or the collateral veins by the spread of thrombophlebitis. These manifestations include pain and tenderness in the lumbar region and the loin and hyperesthesia in the distribution of the lumbar nerves. We believe ligation of the vena cava is indicated when these factors are present, as in the cases described.

REPORT OF CASES

CASE 1.—A white youth of 17 was admitted to an Army and Navy general hospital on Sept. 3, 1946 with severe acute anterior poliomyelitis. Because of respiratory involvement he was immediately placed in a respirator, in which he remained for thirteen days; by the fifteenth day the respirator was no longer necessary. The involvement of the legs remained massive and was associated with severe muscular pains. On the twenty-fourth day after admission he first complained of pain in the right lower quadrant of the abdomen and in the right

*Formerly Major, Medical Corps, Army of the United States.

inguinal region. The temperature was 99 F., and the pulse rate was elevated to 96 beats per minute. Moderate tenderness was present in the right lower quadrant of the abdomen and in the right inguinal region; a greater degree of tenderness was noted over the femoral vessels. There was definite swelling of the right lower extremity. The leukocyte count was 15,700 per cubic millimeter, with a moderate shift to the left. A paravertebral block was performed on the right side, and therapy with heparin sodium and dicumarol® was begun.

On the following day, the patient was seen for the first time by the members of the surgery section; he then complained of increased pain in the thigh, the groin, and the right lower quadrant of the abdomen, and he had become nauseated.

Legs of the patient in case 1 ten months after operation. The patient had been on his feet, wearing long leg braces, for approximately one hour and had been sitting up with his legs dependent for approximately one-half hour before the photograph was taken.

Pronounced tenderness was present in the femoral and right inguinal regions and in the right lower quadrant of the abdomen, and the tenderness had extended into the right flank. The patient also was beginning to complain of some pain in the flank. There was hyperesthesia in the dermatomes supplied by the first to the fourth lumbar spinal nerves. Rectal tenderness was present, mostly on the right side. The diagnosis of thrombophlebitis seemed certain, and it was believed that there was extension into the right iliac vein. Dicumarol® therapy was continued. Findings on the second day after the onset of the pain were unchanged except

for increased pain and tenderness in the loin and beginning pain and tenderness in the left inguinal region. However, on the third day after onset the patient had a sudden severe pain in the right side of the chest accompanied with dyspnea, and he coughed up small amounts of blood-stained sputum. Rales were heard in the base of the right lung. As it seemed certain that he had had a pulmonary embolus, operation was carried out. Procaine hydrochloride (novocain®) was used for local anesthesia. A transperitoneal approach through a right transverse incision spared the inferior epigastric vessels. The right iliac vein was found to be occluded, the clot extending to the bifurcation and just into the left iliac vein, as well as into the vena cava. There was a moderate inflammatory reaction, with edema throughout the area involved, extending around the vena cava to a distance of about 1.5 cm. above the bifurcation. The peritoneum was incised over the vena cava, the vessel freed and a curved clamp passed around it; the clamp was then withdrawn with an umbilical tape, which was tied down firmly. Closure was carried out with silk. The postoperative course was uneventful except for distention, which was controlled without great difficulty. The swelling

TABLE 1.—*Circumference of Legs Before and After Ligation of the Vena Cava in Two Cases*

	Days Before Operation			Days After Operation											
	3	2	1	0	1	2	3	4	5	6	7	8	9	10	11	12
Case 1																
Right leg....	18.5*	20	20	20	20.2	20.5	20	18.7	19	18.7	18.6	18.5	....	18.25	....	18†
Left leg.....	17.0	17.5	17.5	17.5	17.5	17.2	16.7	16.5	16.5	16.9	16.6	16.1	....	16	....	16
Case 2																
Right leg....	....	17.0	17.0	17.5	19	19.5	20	20	20	19	18.7	18.5	18.5	17.8	17.5	17.2‡
Left leg.....	....	17.3	19.0	20	21	22	22	21.5	21	20.5	20	19	19.2	18.5	18	17.7

* All measurements are given in inches.

† Measurements were next taken three months after operation, at which time both legs were 15.5 inches in circumference.

‡ The size of the genitalia had also returned to normal at this time.

of the legs increased only slightly after the operation and then slowly decreased, as shown in table 1. Despite the extremely poor muscular function necessitating his wearing braces, the patient showed no observable dependent edema, as indicated in the photograph. A roentgenoscopic examination with iodopyracet injection (diodrast®), made five months after the operation, showed no evidence of obstruction.

CASE 2.—A white man of 26 sustained a fracture of the twelfth dorsal vertebra with resultant complete paraplegia on Oct. 12, 1946 and was admitted directly to the hospital. On the eighth day after admission, swelling of the left ankle developed, thought to be due to a phlebothrombosis. By the next day, the swelling had extended up through the calf into the thigh. A course of heparin sodium and dicumarol® was begun. Later that day the patient began to complain of lower abdominal pain, and a general consultation concerning operation was held. At that time, there was pronounced edema of the left lower extremity, moderate edema of the scrotum and questionable swelling of the right lower extremity, established by measurement (table 2). There was tenderness in the lower part of the abdomen, especially in the left lower quadrant, and also in the left loin, where it was associated with some muscular spasm. The rectal examination showed tenderness on the left side. The temperature was 99 F., the pulse rate 100 beats

TABLE 2.—*Cases of Ligation of the Inferior Vena Cava Reported in the Literature*

Observer	No. of Cases	No. of Post-operative Deaths	Indication for Ligation	Date
Kocher, cited by Pfaff [27] and Northway and Burton [23]	1	1	Accidental	1883
Billroth, cited by Pfaff,[27] Northway and Burton,[23] and Kern and Berman [19]	1	1	Hemorrhage from operative tear of vena cava	1885
Bottini, E.: Clin. chir. **12**: 529, 1893	1	0	Hemorrhage from operative tear	1893
Héresco, P.: Proc. A. franç. d'urol. **8**: 777, 1905; cited by Miller [13] and Homans, J.: New England J. Med. **211**: 993, 1934	1	0	Hemorrhage from operative tear	Before 1905
Albarran, cited by Kern and Berman [19]	1	0	Hemorrhage from operative tear	Before 1905
Houzel, G.: Rev. de chir. **27**: 455, 1903	1	0	Hemorrhage from operative tear	1903
Hartman, H.: Bull. et mém. de la Soc. nat. de chir. **20**: 57, 1904	1	0	Hemorrhage from operative tear	1904
Trendelenburg, F.: J. A. M. A. **47**: 81 (July 14) 1906; also cited by Moses [9] and Miller [13]	3	2	Pelvic thrombophlebitis	1904 1906
Kohts, K.: Deutsche med. Wchnschr. **37**: 666, 1911; also cited by Kern and Berman [19]	1	0	Hemorrhage from operative tear	1911
Bejan, I., and Cohn, M.: Rev. de chir. **43**: 302, 1911	1	0	Hemorrhage from operative tear	1911
Fromme, cited by Miller [13] and Ochsner, A., and DeBakey, M.: New England J. Med. **235**: 207, 1941	1	1	External thrombosis of the iliac vein	Before 1925
Pfaff [27]	1	0	Hemorrhage from operative tear	1926
Patel, J.: Lyon chir. **24**: 609, 1927	1	0	Hemorrhage from operative tear	1927
Dannheisser, F.: Zentralbl. f. Chir. **54**: 2696, 1927	1	0	Hemorrhage from operative tear	1927
Schroeder, R.: Deutsche med. Wchnschr. **53**: 906, 1927	1	0	Desired removal of thrombus in the inferior vena cava	1943
Atlas, L. N.: Ohio State M. J. **39**: 917, 1943	1	0	Thrombophlebitis extending into the vena cava	1943
Collins, Jones and Nelson [17]	8	1	Pelvic thrombophlebitis	1943
Collins, Jones and Nelson, cited by Ochsner [18]	12	0	Pelvic thrombophlebitis	1945
Ochsner and DeBakey [1]	3	0	Pelvic thrombophlebitis	1944
Kern and Berman [19]	1	0	Septic embolism associated with thrombophlebitis	1945
Burton and Coller [21]	7	0	Long-standing edema and phlebitis of legs, with and without ulceration	1945
Gaston and Folsom [20]	2	0	Thrombophlebitis with multiple emboli (1); continued pulmonary infarction after ligation of both femoral veins	1945
O'Neil [22]	8	0	Ascending thrombophlebitis (5); pulmonary embolism, source unknown (3)	1945
Northway and Burton [23]	10	0	Multiple pulmonary emboli (3); chronic edema of the leg without ulceration (4); chronic edema of the leg with ulceration (2); epigastric pain associated with phlebothrombosis (1)	1945
Kidd, H. A.: Brit. Surg. **73**: 606, 1947	1	0	Injury to inferior vena cava by a bomb splinter	1945

TABLE 2.—*Cases of Ligation of the Inferior Vena Cava Reported in the Literature—Continued*

Observer	No. of Cases	No. of Postoperative Deaths	Indication for Ligation	Date
Veal and Hussey [26]	6	0	Bilateral thrombosis and emboli of the iliac vein (4); extension of inflammation from the left common iliac vein to the vena cava with embolism (2)	1945
Moses [8]	21	*	(Includes both groups described at left.) Recurrent emboli after bilateral ligation of the femoral vein (2); thrombosis of pelvic veins and infarction (2); pulmonary emboli associated with venous clot, fixed to the wall of the femoral vein and extending into the iliac vein (17); venous clot adherent to the femoral vein and extending into the iliac vein without emboli (11); phlebitis of the prostatic veins associated with emboli (11); pulmonary embolism associated with venous occlusion of lower vessels (usually treated by ligation of the femoral vein alone, but contraindicated in these cases by disease in the groin [2])	1946
Fraser, R. W.: Bull. U. S. Army M. Dept. **5**: 357, 1946	1	0	Hemorrhage from the inferior vena cava secondary to shrapnel wound	1948
Thebout, B. R., and Ward, C. S.: Surg., Obst. & Gynec. **84**: 385, 1947	36	4	Thromboembolism	April 1947
Shafiroff, B. G. P.: Am. J. Surg. **73**: 621, 1947	1	0	Bilateral thrombophlebitis with embolism	May 1947
Kirk, G. D.: Am. J. Surg. **73**: 606, 1947	1	1	Extensive septic thrombophlebitis	May 1947

* Reported 6 deaths in 21 ligations of the vena cava and 15 ligations of the common iliac vein.

per minute and the leukocyte count 13,700 per cubic millimeter. The dicumarol® therapy was discontinued, and vitamin K was given. An operation was performed under local anesthesia, as outlined in case 1, except for the use of a left transverse incision. The patient had increased edema, especially of the scrotum, for the first few days after the operation, but it rapidly subsided; by the twentieth day the size of the legs had returned practically to normal. The patient was transferred to another hospital two months after the operation, and other studies have not been possible.

COMMENT

No discussion of surgical treatment of thrombophlebitis or phlebothrombosis of the lower extremity of the pelvic veins would be complete without mention of the importance of prophylaxis against this serious condition. It is our feeling and apparently that of many writers (Ochsner and DeBakey,[1] Potts and Smith,[2] Hunter and others [3] and

1. Ochsner, A., and DeBakey, M.: Thrombophlebitis and Phlebothrombosis, in Lewis, D.: Practise of Surgery, Hagerstown, Md., W. F. Prior Company, Inc., vol. 12, chap. 5-B.

2. Potts, W. J., and Smith, S.: Pulmonary Embolism: An Experimental Study of Variations in the Volume of Blood Flow in the Inferior Vena Cava of the Dog, Arch. Surg. **42**:661 (April) 1941.

3. Hunter, W. D.; Krygier, J. J.; Kennedy, J. C., and Sneedon, V. D.: Etiology and Prevention of Thrombosis of the Deep Leg Veins, Surgery **17**:178, 1945.

Dock [4]) that adequate prophylaxis would prevent most occurrences of this condition, with its severe and often fatal complications. Furthermore, we believe that thrombosis in our surgical cases occurred only when patients were uncooperative in their routine or when some one of the necessary conditions to be described had not been carefully provided. Certainly, the 2 patients whose cases are reported did not have adequate prophylactic treatment.

Adequate prophylaxis includes the following: (1) preoperative preparation, with restoration of the body fluids and the circulation to normal; (2) careful placement of the patient on the table to prevent blocking of the venous return; (3) care in the operative technic, including atraumatic surgery, with the use of fine suture material and the avoidance of mass ligatures, the avoidance of damage to tissues and the prevention of shock, and (4) postoperative care, including an adequate, steady intake of fluids (to maintain venous filling) and continued postoperative exercises, commencing as soon as reaction has occurred. We believe that complete motion of both arms and both legs and deep breathing, performed at least twenty times every hour, is necessary. We feel that if such a regimen is carefully carried out thrombosis will be extremely rare and the occurrence of pulmonary emboli even less common. Other measures which have been advocated are use of the Trendelenburg position after the operation, and early ambulation. These factors have been stressed by Ochsner and DeBakey,[1] Frykholm,[5] Potts and Smith,[2] Hunter and others [3] and Dock.[4]

Early ambulation is used regularly in our cases, but we feel that its use does not decrease the necessity for the foregoing measures. It is our opinion that the few instances of thrombosis which we have observed occurred when the patients were uncooperative or were not encouraged sufficiently in their early postoperative exercises.

The use of heparin sodium and dicumarol® has been urged as a prophylactic measure but would seem to us too dangerous for general use (Ochsner and DeBakey,[1] Barker and others [6] and DeTakats and Fowler [7]). The use of these drugs in treatment has been extensive, but there are dangers, especially that of severe or fatal hemorrhage, as in Moses' 2 cases,[8] and the action of the drugs is difficult to control. Fur-

4. Dock, W.: The Use and Abuse of Bed Rest: Conferences on Therapy, New York Hospital, N. Y. State J. M. **44**:724, 1944.

5. Frykholm, R.: Pathogenesis and Mechanical Prophylaxis of Venous Thrombosis, Surg., Gynec. & Obst. **71**:307, 1940.

6. Barker, N. W.; Hygaard, K. K.; Walters, W., and Priestley, J. T.: A Statistical Study of Postoperative Venous Thrombosis and Pulmonary Embolism: Predisposing Factors, Proc. Staff Meet., Mayo Clin. **16**:1, 1941.

7. DeTakats, G., and Fowler, E. F.: The Problem of Thrombo-Embolism, Surgery **17**:153, 1945.

8. Moses, W. R.: Ligation of Inferior Vena Cava or Iliac Vein, New England J. Med. **235**:1, 1946.

thermore, they do not definitely prevent pulmonary emboli, even with adequate dosage, as stated by Ochsner and DeBakey [1] and as shown in our case 1. In the group of men who oppose their use are Moses,[8] Homans,[9] and Fine and Starr.[10] Those who favor their use include Barker, Nygaard, Walters and Priestley,[6] and de Takats and Fowler.[7] Our own feeling is that they are a valuable adjunct, to be used only with great care and with an excellent laboratory service available.

HISTORY

Apparently the first ligation of the inferior vena cava was performed accidentally by Kocher in 1883 and was recognized only at postmortem examination. The first intended ligations were necessitated by operative injury to the vena cava; Trendelenburg's 3 cases (Trendelenburg,[11] Moses [8] and Miller [12]) of ligation for pelvic thrombophlebitis were exceptions. Only 1 of these 3 patients survived. Eighteen cases were collected by Pleasants [13] in 1918. Excellent reviews were made by Petit [14] in 1926 (11 cases with 4 deaths), by Wakefield and Mayo [15] and by Krotoski [16] in 1937. Our own review of the literature as available is briefly outlined in table 2.

INDICATIONS AND RESULTS

As in most surgical conditions, there are a few absolute indications and contraindications for a certain procedure, with a middle ground where strong difference of opinion exists.

The absolute indications for ligation of the inferior vena cava, in addition to injury to the vein, appear to be the following: (1) pelvic thrombophlebitis or infected thrombi (Collins, Jones and Nelson,[17]

9. Homans, J.: Deep Quiet Venous Thrombosis in the Lower Limb: Preferred Levels for Interruption of Veins; Iliac Section or Ligation, Surg., Gynec. & Obst. **79**:70, 1944.

10. Fine, J., and Starr, A.: Surgical Therapy of Thrombosis of the Deep Veins of the Lower Extremities, Surgery **17**:232, 1945.

11. Trendelenburg, F.: Ueber die chirurgische Behandlung der puerperalen Pyämie, München. med. Wchnschr. **49**:513, 1902.

12. Miller, C. J.: Ligation or Excision of Pelvic Veins in Treatment of Puerperal Pyemia, Surg., Gynec. & Obst. **25**:1431, 1917.

13. Pleasants, J. H.: Obstruction of the Inferior Vena Cava: Report of Eight Cases, Johns Hopkins Hosp. Reports **16**:363, 1911.

14. Petit, J.: Des plaies opératoires de la veine cava inférieure, J. chir. rev. critique **9**:153 (July-Dec.) 1912.

15. Wakefield, E. G., and Mayo, C. W.: Obstruction of Vena Cava Distal to Renal Veins, J. Missouri M. A. **31**:92, 1934.

16. Krotoski, J.: Zur Venenunterbindung bzw. -extirpation bei der puerperalen Allgemeininfektion vom chirurgischen Standpunkt, Chirurg. **9**:425, 1937.

17. Collins, C. G., Jones, J. R., and Nelson, E. W.: Surgical Treatment of Pelvic Thrombophlebitis: Ligation of Inferior Vena Cava and Ovarian Veins; Preliminary Report, New Orleans M. & S. J. **95**:324, 1943.

Ochsner and DeBakey,[1] Ochsner,[18] Kern and Berman,[19] and Moses [8]); (2) saddle thrombi, and (3) emboli following bilateral ligation of the femoral artery (Gaston and Folsom [20]). Moses stated that the inferior vena cava should be ligated for thrombophlebitis of the pelvis with "pulmonary embolus associated with prostatic tenderness of recent, or presumably recent, origin, especially with demonstration of deep tenderness along the anterolateral region of the rectum; reasonably conclusive evidence of pulmonary infarcts the source of which remains obscure despite diligent search; and venous occlusion of the lower extremities that would otherwise be treated by interruption of the femoral vein alone. The conditions governing the last are as follows: cellulitis or lymphangitis of the upper thigh, infections of the groin or the finding of enlarged and tender inguinal or femoral-triangle lymph nodes; recurrent emboli following bilateral ligation of the femoral veins; femoral phlebothrombosis with tense edema extending above the knee; the operative findings of adherent clot on exposure of the femoral vein; and acute thrombophlebitis extending into the upper thigh clinically, with the presence of pulmonary embolism."

In contradistinction, there would seem to be little indication for this procedure in unilateral phlebothrombosis or in thrombophlebitis which has not extended beyond the femoral vein.

In our 2 cases, we observed certain signs which had not been stressed previously. With progression of the disease process, inguinal pain and then lower abdominal pain (both of which have been mentioned repeatedly in the literature) developed; the pain then rapidly extended high into the lumbar region and the loin. It was associated with pronounced tenderness in the same area, with muscular spasm and with hyperesthesia in the distribution of the lumbar dermatomes. Although we have no anatomic proof, it is our belief that these symptoms and signs indicate a spread of the occlusive process into the vena cava or the lumbar collateral veins and so are a direct indication for ligation of the vena cava.

It is particularly in those cases of silent emboli, bilateral involvement of the lower extremity and involvement of one or both iliac veins or associated inflammation of the thigh or groin (Moses [8]) that a difference of opinion exists. Recently, chronic, deep phlebitis with edema of the legs has become an additional indication for ligation of the vena cava (Burton and Coller [21] and Kern and Berman [19]).

---

18. Ochsner, A.: Intravenous Clotting, Surgery **17**:240, 1945.

19. Kern, H. M., and Berman, E.: Ligation of Inferior Vena Cava for Pneumonic Thrombophlebitis, Am. J. Surg. **69**:120, 1945.

20. Gaston, E. A., and Folsom, H.: Ligation of Inferior Vena Cava for Prevention of Pulmonary Embolism: Report of Two Cases, New England J. Med. **233**:229, 1945.

21. Burton, R. W., and Coller, F. A.: Surgical Treatment of Long Standing Deep Phlebitis of the Leg, Surgery **18**:663, 1945.

Moses,[8] O'Neil[22] and Northway and Burton[23] stated the belief that ligation of the vena cava is indicated in cases of silent emboli, whereas Homans[9] was opposed, preferring bilateral ligation of the femoral vein. It must be remembered that bilateral thrombus formation occurred in a high percentage of cases; Neuman[24] recorded 52 per cent in postmortem studies. In the series of 202 cases recorded by Allen and others,[25] 78 per cent of ligations of the femoral vein were bilateral, and Fine and Starr[10] advocated routine bilateral ligation of the femoral vein. Concerning extension of the bilateral involvement to the inguinal ligament or above, opinion favored ligation of the vena cava (Homans,[9] Wakefield and Mayo[15] and O'Neil[22]).

It is our belief that even with involvement of one iliac vein ligation of the vena cava is the procedure of choice; this was the opinion of Moses,[8] Wakefield and Mayo[15] and O'Neil.[22] It was opposed by Homans,[9] Fine and Starr[10] and Veal and Hussey,[26] who stated that ligation of the iliac vein was indicated. The primary reason for ligation of the iliac vein is fear of a reduction in venous return after ligation of the vena cava; this has been fairly well disproved. O'Neil[22] stated that the collateral circulation after ligation of the vena cava is in effect as adequate as that after ligation of the common iliac vein: "The collateral pathways available after ligation of the lower vena cava fall roughly into three groups—the superficial, the deep, and those of the ascending lumbar trunks. The first of these comprise the superficial circumflex iliac and the superficial epigastric veins, which connect the saphenous system with the superficial thoracic veins and those of the upper abdominal wall. The deep pathways are formed by the anastomosis of the deep circumflex iliac, superior epigastric and lumbar veins, thereby connecting the external iliac veins with the internal mammary and ascending lumbar veins. The ascending lumbar trunks begin in the pelvis on either side of the promontory of the sacrum and communicate with the sacral common iliac, hypogastric and iliolumbar veins. . . . The right lumbar trunk becomes the azygos vein and terminates in the superior vena cava; the left continues as the hemiazygos vein and eventually enters the right azygos vein." Experiments with injection

22. O'Neil, E. E.: Ligation of the Inferior Vena Cava in Prevention and Treatment of Pulmonary Embolism, New England J. Med. **232**:641, 1945.

23. Northway, R. O., and Burton, R. W.: Ligation of Inferior Vena Cava, Surgery **18**:85, 1945.

24. Neumann, R.: Ursprungszentren und Entwicklungsforsmen der Beinthrombose, Virchows Arch. f. path. Anat. **301**:708, 1938.

25. Allen, A. W.; Linton, R. R., and Donaldson, G. A.: Thrombosis and Embolism: Review of Two Hundred and Two Patients Treated by Femoral Vein Interruption, Ann. Surg. **118**:728, 1943.

26. Veal, J. R., and Hussey, H. H.: Deep Venous Thrombosis of the Lower Extremities, Surgery **17**:218, 1945.

by Bohner, Poirer and Goleman, cited by Kern and Berman,[19] showed that after ligation of the vena cava the blood is returned to the heart without difficulty; this fact was confirmed in our case 1 by a roentgenoscopic examination after the administration of iodopyracet injection. Northway and Burton,[23] using injection methods in the study of cadavers, observed the more important collateral pathways and proved that they were obviously adequate. (The principal anastomotic channels are veins in and about the spinal canal, the groin and the azygos veins.)

In Northway and Burton's 10 cases in which ligation was done, any edema of the legs which persisted was well controlled with elastic bandages; the degree of immediate postoperative edema was minimal. Moses [8] stated that whenever edema follows ligation of the vena cava or the iliac vein there is unequivocal evidence of either persistence or recurrence of the disease process. He also stated the belief that edema of the leg is less severe after ligation of the vena cava than after ligation of the femoral vein. Kern and Berman's patient [19] was free of edema on the sixteenth day; later, he was able to work as a policeman without discomfort, edema or the necessity for an elastic stocking. Others supported this evidence with case reports (O'Neil,[22] Gaston and Folsom,[20] Pfaff [27] and Veal and Hussey [26]). Further studies on venous pressure by Collins, Jones and Nelson [17] showed a rapid fall in venous pressure in the first weeks after ligation. In our 2 cases, edema disappeared in eleven and ten days, respectively. In support of Moses' contention,[8] the patient in case 1 showed rapid subsidence of the swelling in the first leg involved; there was slightly increased edema of the other leg, evidently due to its thrombotic involvement, but this also subsided (over a period of twelve days) until the leg was smaller than it had been before the operation (table 1).

Another factor in favor of ligation of the vena cava rather than of one iliac vein is the high incidence of bilateral involvement. Ligation of the vena cava prevents the formation of an embolism from the other leg. Veal and Hussey [26] reported 3 cases in which death occurred from this cause. Since the two procedures are similar in time, skill and amount of anesthesia necessary as well as in risk, ligation of the vena cava seems the procedure of choice. Actually, to us, it seems an easier procedure, especially if the left iliac vein is involved. Hershey and Bailey [28] used ligation of the vena cava in their case because of the patient's poor condition, and stated that they ordinarily would have used ligation of the iliac vein. If it is used in cases of poor risk

27. Pfaff, O. G.: Ligation of Inferior Vena Cava, Am. J. Obst. & Gynec. **11**:660, 1926.

28. Hershey, C. D., and Bailey, R. D.: Management of Thrombophlebitis, West Virginia M. J. **42**:1, 1946.

because it is easier, why should it not be used in all cases? Veal and Hussey [26] reported 4 cases in which the formation of recurrent pulmonary emboli followed ligation of the femoral vein through a diseased segment, and other cases in which a thrombus formed above the point of ligation and extended into the inferior vena cava, making a secondary and more hazardous operation necessary. Certainly, primary ligation of the vena cava would seem the most conservative operation in such cases. Apparently no deaths occurred in the 6 cases of ligation of the vena cava reported by Veal and Hussey; there were 7 among 76 other cases.

So far as the operative technic itself is concerned, we favor the transperitoneal approach for its simplicity. A short transverse or midline incision should be used in order to save the inferior epigastric vessels for collateral circulation. The intestines are packed away. A short incision is made through the posterior peritoneum overlying the vena cava, the peritoneum is stripped off and a curved instrument is passed around the vein with the ligature, which is then slowly drawn tight. In each case, the ligation was made just above the last lumbar vein. It is easier here, and we thought that the presence of the lumbar vein below the ligature might assist in the formation of late collateral circulation. Umbilical tape was used, but any suture large enough to prevent cutting of the vein will suffice. The advantages of this approach over the retroperitoneal approach are: (1) ease of observation of pathologic features, (2) preservation of all the lumbar veins for collateral circulation (they may be torn or traumatized in the retroperitoneal approach), (3) performance of the procedure entirely under direct vision and (4) ease of performance of a lumbar sympathectomy, if it is indicated.

Any anesthesia indicated for the patient is satisfactory. In our cases, a 1 per cent solution of procaine hydrochloride was used locally because of the patient's extremely poor condition.

SUMMARY

Thrombosis, either postoperative or occurring in the course of medical diseases, is a serious complication, primarily because of the frequent deaths due to pulmonary embolus and secondarily because of the residual edema and ulceration of the leg. The prevention of thrombosis is made possible in most instances by careful prophylactic measures, including the maintenance of fluid balance, the prevention of stasis, the prevention of shock and, in surgical cases, the use of technic to minimize damage to the tissues. The use of conservative measures, as indicated, will prevent any serious complication in most instances. These should include the immobilization and elevation of the leg and the use of a heat cradle, supporting (elastic) bandages and perhaps, sympathetic nerve blocks. We feel that the use of anticoagulant drugs

is indicated in a certain percentage of cases. Surgical measures will be necessary in a small percentage of cases, including ligation of the femoral vein of either type, as indicated, and rarely, ligation of the iliac vein on the right side or of the vena cava. When the thrombosis has spread into the left iliac vein, or into either iliac vein with a possibility of involvement of the opposite leg, we believe that ligation of the vena cava is the procedure of choice. We believe that ligation of the vena cava is indicated in cases in which there is involvement of both legs to above the inguinal region and in cases of pelvic thrombophlebitis because of the ease of access, the lack of trauma to the tissues and the ease of observation of pathologic conditions.

ADDITIONAL REFERENCES

Bancroft, F. W.: Proximal Ligation and Thrombectomy for Phlebothrombosis of the Femoral and Iliac Veins, Ann. Surg. **121**:175, 1945.

Bauer, G.: Venographic Study of Thromboembolic Problems, Acta chir. Scandinav. (supp. 61) **84**:1, 1940.

Belt, T. H.: Thrombosis and Pulmonary Embolism, Am. J. Path. **10**:129, 1934.

Cole, H. P.: Laceration of Inferior Vena Cava: Repaired by Suture with Recovery, Ann. Surg. **66**:43, 1917.

Costa, G.: Contributo allo studio delle ferite della vena cava inferiore, Arch. ital. de chir. **4**:339, 1921.

Cumston, C. G.: The Treatment of Wounds of the Vena Cava During Nephrectomy, New York M. J. **82**:77, 1905.

Deraw, H. A.; Schlesinger, M. J., and Savitz, H. A.: Chronic Progressive Occlusion of Inferior Vena Cava, Arch. Int. Med. **63**:626 (April) 1939.

Goldmann, E. E.: Ueber die Unterbindung von grossen Venenstämmen, Beitr. z. klin. Chir. **47**:162, 1905.

Gosset, A., and Lecene, P.: A propos de la ligature brusque de la veine cava inférieure, Tribune méd. **36**:213, 1904.

Hartman, J.: Puerperales Pyämie bei Unterbindung der Vena cava inferior, München med. Wchnschr. **58**:711, 1911.

Henderson, E. F.: Fatal Pulmonary Embolism: Statistical Review, Arch. Surg. **15**:231 (Aug.) 1927.

Huggins, R. R.: Ligation or Excision of Ovarian or Deep Pelvic Veins in Treatment of Puerperal Thrombophlebitis, J. A. M. A. **59**:160 (July 20) 1912.

Husten, K.: Anatomische und histologische Untersuchungen über Weite und Wand der Hohlvenen unter psychologischen und pathologischen Kreislaufbedingungen, Vienna, G. Fischer, 1926, p. 84.

Hyman, A., and Leiter, H. E.: Surgery of the Inferior Vena Cava in Genito-Urinary Conditions, J. Urol. **45**:813, 1941.

Kocher, T.: Text Book of Operative Surgery, New York, The Macmillan Company, 1911, vol. 1, p. 162.

Loewe, L.; Rosenblatt, P., and Hirsch, E.: Venous Thromboembolic Disease, J. A. M. A. **130**:386 (Feb. 16) 1946.

McCartney, J. S.: Post Operative Pulmonary Embolism, Surgery **17**:191, 1945.

Moses, W. R.: Early Diagnosis of Phlebothrombosis, New England J. Med. **234**:288, 1946.

Pilcher, L. S.: Treatment of Pulmonary Embolism, Am. J. Surg. **69**:190, 1945.

Priestly, J. T., and Barker, N. W.: Post Operative Thrombosis, Surg., Gynec. & Obst. **75**:193, 1942.

Rössle, R.: Ueber die Bedeutung und die Entstehung der Wadenvenenthrombosen, Virchows Arch. f. path. Anat. **300**:180, 1937.

Sears, J. B.: Experiments with Femoral Vein Ligation for Prophylaxis of Post Operative Emboli, New England J. Med. **224**:108, 1941.

Shackelford, R. T., and Whitehill, R.: Successful Ligation of Left Common Iliac Vein for Thrombophlebitis Complicated by Pulmonary Emboli, Bull. Johns Hopkins Hosp. **73**:307, 1943.

Walters, W., and Priestley, J. T.: Surgery of the Inferior Vena Cava, Ann. Surg. **99**:167, 1934.

Weber, F. P.; Post, H., and Wandt, G.: Thrombosis of Inferior Vena Cava: Prognosis, M. Press. **196**:262, 1938.

Welch, C. E., and Faxon, H. H.: Thrombophlebitis and Pulmonary Embolism, J. A. M. A. **117**:1502 (Nov. 1) 1941.

Weinstein, B. B., in discussion on Collins, C. G.; Jones, J. R., and Nelson, E. W.: Surgical Treatment of Pelvic Thrombophlebitis, N. Orleans M. & S. J. **95**:324, 1943.

Whittenberger, J. L., and Huggins, C.: Ligation of Inferior Vena Cava, Arch. Surg. **41**:1334 (Dec.) 1940.

SIGNIFICANCE OF THE SEROSAL ARTERIOLES IN RESUSCITATION OF THE SMALL BOWEL

BERNARD J. FICARRA, M.D.
Professor in Charge of Experimental Physiology, St. Francis College
BROOKLYN

ON MANY occasions the surgeon is confronted with the problem of whether or not an intestinal segment is viable. This is especially true in emergency situations, as when an operation is performed for incarcerated and/or strangulated hernias or for intestinal obstruction. At the operating table valuable time elapses as the surgeon waits patiently to ascertain the return of a bowel loop to normalcy. Since most patients with these conditions are not the best operative condidates, the additional period of anesthesia and exposure of the peritoneal cavity to the atmosphere increases the morbidity. Often this delay, lingering and waiting, is a major factor in producing death.

Thus a rapid diagnostic criterion of viability of the small bowel is of practical importance. Observation at the operating table in this type of situation has brought to light such a criterion. In addition to the clinical observation, experimental evidence in animals is offered in support of it.

The final test of whether or not a loop of small intestine is viable depends primarily on the blood supply to that loop. A basal blood supply which can maintain the nutritional state of the intestinal wall is sufficient to preserve viability. This blood supply may be adequate even in the presence of local intestinal cyanosis, congestion and inhibited peristalsis. Obstructed loops of small intestine have a remarkable inherent potentiality of returning to normal. However, in the presence of advanced thrombosis in the mesenteric vessels, or bowel asphyxia, resuscitation is impossible. Therefore a correct indicator of adequate blood supply to the bowel segment is the all-important determinator. This determinator enables the observer to know that resuscitation of the bowel will occur even in the presence of marked congestion, discoloration and inhibition of peristalsis. Hence, if this indicator is adequate, a questionable intestinal loop may be redeposited immediately into the peritoneal cavity without undue fear of perforation.

It is believed that a satisfactory determinator of this type is available to the surgeon at the operating table. This indicator is visible by direct investigation of the vascular tree. The point of observation is the most

From the Department of Surgery, Kings County Hospital.

distal circumference of the small intestine on the antemesenteric border. The serosal arterioles are examined for their red color and the presence or absence of pulsations. These vessels in normal intestine are not as prominent as they are in the obstructed loop with secondary venous congestion. The venous congestion increases the arteriolar pressure so that the vessels become extremely prominent. If pulsations are visible in the small arterioles on the antemesenteric border and if the red color of the circulating blood can be seen, the bowel is viable. This is true

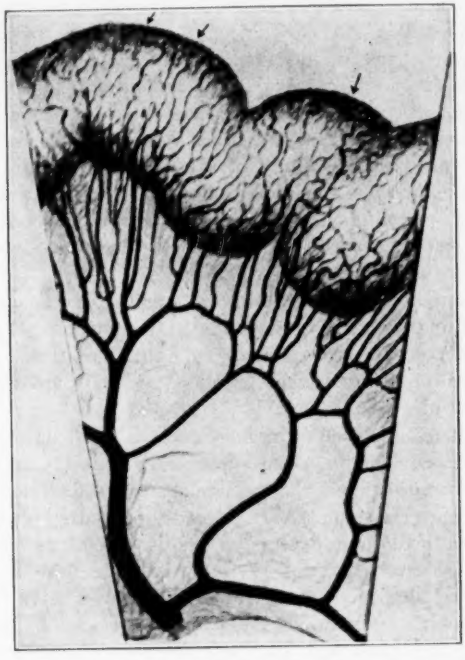


Fig. 1.—Injected arteries of human ileum demonstrating the rich vascularity of the small bowel. Arrows indicate the point of observation in the determination of the viability of the intestinal segment.

even if the intestinal wall is markedly darkened from edema and congestion and even if the blue-black color of the intestine is prominent.

The rationale of this observation resides in the fact that if there is adequate arterial circulation and venous return in the most distal area of the intestine the circulation must be satisfactory in the more proximal areas. Where there is adequate arterial circulation, there is also adequate oxygenation with a satisfactory nutrition supply to the tissue under

Fig. 2.—Intestinal loop demonstrating the return to normal of an obstructed segment of bowel in a rabbit. Serosal arterioles are visible, indicating adequate blood supply.

observation. Adequate oxygenation and nutrition of the segment are the basic necessities for intestinal viability. Both these physiologic functions depend on a sufficient arterial circulation. Therefore, when an adequate circulation is present, the intestine must, of necessity, be viable. This criterion has been followed on many occasions at the operating table without any serious complications occurring which could be attributed to the intestinal segment under observation.

In order to substantiate this clinical observation, experimental evidence is offered in its support. The animals employed for study were rabbits in whom occlusion of the blood supply to intestinal segments was artificially induced. Strangulation of the intestine was allowed to progress until the arterioles of the antemesenteric border became prominently visible. The intestine became blue-black and congested, and peristalsis was inhibited. When this point was reached, the blood supply was allowed to return, and the intestinal loop regained its former appearance. The rabbit's abdominal wall was sutured, and each animal had an uneventful recovery. This procedure was performed in 3 different rabbits.

The same procedure of obstructing an intestinal loop was performed with the exception that strangulation of the bowel was allowed to continue beyond the preservation of the arteriolar blood supply. Obstructed segmental loops of this type could not and did not return to normal. This is the type of strangulated intestine which goes on to perforation producing peritonitis. Three rabbits were treated in this fashion. All died. Autopsy revealed generalized peritonitis secondary to intestinal gangrene with perforations. Thrombotic processes were evident in the vascular tree of the segments involved.

This experimental evidence and clinical observation on strangulation of the small intestine has unfolded a diagnostic criterion of determining the viability of strangulated intestine in the operating room. This criterion enables the surgeon to save valuable time as he attempts to determine the viability of obstructed intestinal loops. Furthermore, it will decrease the period of exposure to which the peritoneal cavity may be subjected. This factor may be the deciding point in the preservation of life in a patient who is already debilitated by a physiologic imbalance secondary to an intestinal obstruction.

SUMMARY AND CONCLUSIONS

1. The need for a decisive, rapid method of determining the viability of small intestine is emphasized.

2. Clinical observation and animal experimentation have supplied a criterion to answer this need.

3. The criterion in question concerns the serosal arterioles on the antemesenteric border of the small bowel.

4. Adequate circulation in these vessels indicates viability of the bowel even in the presence of discoloration, edema and inhibition of peristalsis.

5. Employing this criterion, the surgeon has available a rapid indicator which will save valuable time in determining the integrity of intestinal loops.

This procedure has been followed without any resulting complication which can be attributed to the unreliability of the diagnostic criterion. It is therefore advocated as a safe and sound method of determining intestinal resuscitation.

PROGRESS IN ORTHOPEDIC SURGERY FOR 1946

A Review Prepared by an Editorial Board of the American Academy of Orthopaedic Surgeons

XIX. FRACTURES

Prepared by

WALTER G. STUCK, M.D.
SAN ANTONIO, TEXAS

DON H. O'DONOGHUE, M.D.
AND
CHARLES R. ROUNTREE, M.D.
OKLAHOMA CITY

RUFUS H. ALLDREDGE, M.D.
NEW ORLEANS
AND
PAUL L. NORTON, M.D.
BROOKLINE, MASS.

IN 1946, the first postwar year, the number of articles on fractures increased and the emphasis shifted from gunshot fractures to more nearly normal interests. Intramedullary fixation continued to attract more attention and represented the principal change in the management of fractures. The use of antibiotic drugs became so general that little more was said about their use in compound wounds. External devices for skeletal fixation were mentioned much less frequently as vitallium plates and screws and "18-8 S M O" stainless appliances came to be recognized for their dependability. But still unsettled were the many questions raised concerning conservative vs. operative treatment of fractures.

FRACTURES OF THE SHOULDER

McBride [868] makes the point that shoulder injuries are not always easy to diagnose and may be confused with lesions of the cervical portion of the spine. Consequently, the diagnosis must be well established before any plan of treatment is undertaken.

Dor [869] had the experience of reducing dislocations of the shoulder in several hundred cases by a simple maneuver, without anesthesia. While he explained to the patient that he was only making an examination, the elbow was brought forward while the wrist was pushed outward; often there was a click as the shoulder fell in place. Sometimes

868. McBride, E. O.: Shoulder Wounds and Injuries, New Orleans M. & S. J. **98**:533-541 (June) 1946.

869. Dor, J.: Reduction of Recent Anterior-Internal Luxations by Slow Rotation, Rev. d'orthop. **32**:197-198 (May-Aug.) 1946.

several repetitions of the maneuver were required before the shoulder was reduced. As the author explains, the method is recommended only for use in cases of recent fracture and after preliminary roentgenographic examination.

A case of bilateral dislocation of the shoulder is reported by Lynn and Peterson.[870] The patient, a navigator on a bomber, was propelled between the seats of the pilot and the co-pilot in a crash landing, sustaining bilateral subcoracoid dislocation. The patient was treated two months after injury by open reductions and Nicola fixation. Preliminary traction for eighteen days on the left shoulder made the operation easier than on the right side, on which no preliminary traction was used. Active motion was started one month after the second operation (seven weeks after the first). Abduction and flexion to 90 degrees bilaterally, with moderate restriction of rotation, was obtained.

Smith [871] reports a rare type of posterior dislocation of the shoulder in a frail woman, of 88, who fell forward without having the arm extended. Arthritic changes present in the joint may have facilitated the displacement, which was easily recognized by palpation and was corrected by the usual Kocher maneuver. In those cases in which the condition is not recognized, a good, functional false joint is established behind the glenoid cavity.

Hart [872] recommends that irreparably injured shoulders be immobilized in a plaster spica, the following factors obtaining: (1) 60 to 70 degrees of abduction; (2) 45 degrees of forward flexion; (3) normal position of the scapula; (4) sufficient external rotation at the shoulder so that the hand is on a level with the chin; (5) extension of the shoulder spica from the crease of the palm to just above the trochanters, so that the spica rests firmly on the pelvis; (6) inclusion in the spica of a strap of plaster over the normal shoulder, and (7) prevention of pressure on the ulnar nerve or the median epicondyle.

Fractures of the Scapula.—Pelloja [873] states that isolated fractures of the acromion are rare. In cases involving young persons, the confusing point in diagnosis is the fact that the epiphysis does not fuse until 20 to 25 years of age. In reports of 2 cases, the author describes the treatment of lateral fractures by lifting and abducting the shoulder.

870. Lynn, T. A., and Peterson, L. T.: Bilateral Simultaneous Dislocations of Shoulders, J. Bone & Joint Surg. **28**:161-163 (Jan.) 1946.

871. Smith, A. M.: Subacromial Dislocation of the Shoulder, Brit. M. J. **2**:694-695 (Nov. 9) 1946.

872. Hart, V. L.: Immobilization of Irreparably Injured Shoulder Joint, Bull. U. S. Army M. Dept. **5**:366 (March) 1946.

873. Pelloja, M.: Isolated Fractures of the Acromion, Arch. ital. chir. **67**:140-146, 1945.

A case of bilateral fracture of the scapula is reported by Heatly, Breck and Higginbotham.[874] One scapula was treated by strapping with adhesive tape, but the other required insertion of skeletal traction along the vertebral border and counter traction through adhesive tape on the arm. Satisfactory, though not perfect, reduction was obtained; the functional result was excellent.

Acromioclavicular Dislocation.—Simple strapping of the acromioclavicular joint was used by Goldberg[875] in 53 cases; all patients were able to return to duty within four weeks. Adhesive tape was passed over a pad on the outer end of the clavicle and down around the padded olecranon; the arm was then fixed to the chest with tape. The patients were thus immobilized from four to fourteen days or until all tenderness had subsided.

Gibbens[876] describes a special type of cast to hold the acromioclavicular joint after dislocation and reduction. A cast is placed on the arm, and two aluminum extension bars are attached to the top of the cast. An elastic strap over the end of the clavicle is fastened to the extension bars in the cast. Results were satisfactory in 10 cases.

Stewart[877] reports 9 cases of acromioclavicular separation; treatment was with the Bosworth vitallium screw, inserted through the clavicle and into the coracoid process.

[ED. NOTE (W. G. S.).—As these articles indicate, there is still no generally accepted treatment for acromioclavicular separation. Strapping, the use of casts, screws, wire or fascial loops and resection of the end of the clavicle are still in vogue with various surgeons. Fortunately, the ill effects of this injury are not particularly disabling.]

Fractures of the Clavicle.—Van Demark and Goodman[878] stress that in treating fracture of the clavicle in soldiers, it is extremely important to secure exact reposition of the fragments. Otherwise the irregular fracture site will be irritated by shoulder straps, rifles and other military equipment. Therefore the authors followed a policy of treating the patients in bed, with lateral traction on the arm for five weeks. Even so, it was sometimes necessary to manipulate the fragments under anesthesia.

---

874. Heatly, M. D.; Breck, L. W., and Higginbotham, N. L.: Bilateral Fracture of the Scapulae, Am. J. Surg. **71**:256-259 (Feb.) 1946.

875. Goldberg, D.: Modified Conservative Treatment of Acromio-Clavicular Joint Injuries, Am. J. Surg. **71**:529-531 (April) 1946.

876. Gibbens, M. E.: Appliance for Conservative Treatment of Acromio-Clavicular Dislocations, J. Bone & Joint Surg. **28**:164-165 (Jan.) 1946.

877. Stewart, R.: Internal Fixation of Clavicle and Coracoid Process with Vitallium Screw, Minnesota Med. **29**:357 (April) 1946.

878. Van Demark, R. E., and Goodman, M. C.: Clavicle Fractures in Military Trainees, Mil. Surgeon **99**:197-199 (Sept.) 1946.

Mbuthia and Kisali [879] treated 300 patients with fracture of the clavicle with figure 8 plaster bandage, applied while the shoulders were held in extension. Temporary symptoms of pressure on the nerve developed in only 1 case.

Goumain and Labarbe [880] describe a method of internal fixation of the clavicle by insertion of a Kirschner pin through a transcutaneous approach. For fixation of a fracture near the outer extremity of the clavicle a puncture wound is made in the skin, and, through it, an oblique opening is made in the clavicle, about 6 cm. from the sternoclavicular joint. The hole is directed backward and outward. After reduction a Kirschner pin, 10 cm. in length, is inserted under radioscopic control, to the peak of the first curvature. If the end of the pin extends beyond the entry hole, it is withdrawn slightly, cut off properly and driven in flush with the bone. The shoulder is mobilized on the second or third day, using a sling. For treatment of fractures of the inner end of the clavicle, the pin is inserted from the acromial end.

Bermudez and Odam [881] state that they treat fractures of the clavicle by reduction under local anesthesia, with the patient in a sitting position. Traction is applied with a knee, between the shoulders, and the clavicle is immobilized by the use of prepared loops of bandage, passed over axillary pads and acromial pads without compression. The arm on the injured side is kept in a sling for about twenty-five days. "The result, though not always perfect reduction, is excellent function."

Lee [882] used a nail, driven in from the outer end of the clavicle through an incision along its upper border, to secure reduction in a case in which repeated attempts at closed reduction had failed. No retention was used. The nail was removed in six weeks, and the result was perfect.

Cobey [883] describes a method used for eleven years with no unfavorable complications. In about 14 per cent of cases in which reduction could not be maintained, an incision was made over the fracture and the fragments were held together with towel clips, forced into the bone. The handles of the towel clips were fastened to each other with a wooden block.

---

879. Mbuthia, A. S., and Kisali, J.: Treatment of Fracture of the Clavicle by Plaster of Paris Bandages, East African M. J. **23**:154-155 (May) 1946.

880. Goumain, A. J. M., and Labarbe: Transcutaneous Intramedullary Fixation of Fractures of the Clavicle with Kirschner Pin, Bordeaux chir. **3-4**:75-80 (July-Oct.) 1943.

881. Bermudez, E., and Odam, J.: Conservative Procedure in Therapy of Fractures of the Clavicle, Gac. méd., Lima **1**:168-169 (June) 1945.

882. Lee, H. G.: Treatment of Fracture of Clavicle by Internal Fixation with Nail, New England J. Med. **234**:222-224 (Feb. 14) 1946.

883. Cobey, M. C.: Towel Clip Fixation of Fresh Clavicular Fractures, South. M. J. **39**:307-311 (April) 1946.

[Ed. Note (W. G. S.).—Of course, most fractures of the clavicle are uncomplicated, and the usual conservative treatment is adequate. Moreover, nonunion is extremely rare in the clavicle, and union in practically any position will give a well functioning shoulder. Therefore, operative treatment should be reserved for the unusual or irreducible fracture of the clavicle.]

FRACTURES OF THE UPPER EXTREMITY

In a comprehensive article, Fitts [883a] presents a digest of treatment of fractures of the upper extremity, gathered chiefly from seventy-seven articles listed in the bibliography. The salient points are: 1. Fractures of the upper extremity in World War II were treated by ambulatory methods. 2. War experience has emphasized that the functioning of the joints of the upper extremity should be subservient to the proper functioning of the hand. 3. Fractures of the humerus were best handled with the arm near the body, and the efficiency of the "hanging cast" was established. 4. A high incidence of fractures of the carpal scaphoid was encountered, good results being obtained by prolonged immobilization if instituted early. 5. Fingers immobilized in extension showed a high incidence of stiffness, indicating that positions of flexion should be used and that the uninjured fingers must not be immobilized. 6. Injuries to nerves and blood vessels were frequent in compound fracture of the upper extremity, and treatment of these injuries often took precedence over treatment of the fracture.

Fractures of the Humerus.—Jones [884] has used a metal abduction splint for fractures of the upper two thirds of the humerus for more than twenty years. It is very light, being made of duralumin, and can be bent easily to conform to the arm and body. Only a slight amount of abduction is needed to correct most deformities of the humerus, and this splint is sufficient in more than 90 per cent of cases.

Kandel [885] discusses the anatomy and function of the normal shoulder and includes a lengthy section on the roentgenography of the region; the types of fractures and of undetermined fractures or dislocations are described from the point of view of a radiologist. The mechanism of the fracture, such as direct blow, torsion or compression, is then discussed. The author states the belief that the mechanism of displace-

883a. Fitts, W. T., Jr.: Fracture of Upper Extremity: Review of Experiences in World War II, Am. J. Surg. **72**:393-403 (Sept.) 1946.

884. Jones, L.: Simple Conservative Method of Treatment of Fractures of the Upper End of the Shaft of the Humerus, Surg., Gynec. & Obst. **83**:126-128 (July) 1946.

885. Kandel, B.: Fractures and Fracture Luxations of the Upper End of the Humerus, Semana méd. **1**:422-447 (March 7) 1946.

ment is due to muscular action; there is a long, detailed section on the manner in which this factor acts.

A discussion of the use of Caldwell's "hanging cast" for treatment of fractures of the humerus is presented by Paredes.[886] The article is devoted to an exposition of the advantages of the method, a review of the muscles inserted on the humerus and the effect of these muscles on fractures at different levels. The author lists the types of fractures to which the method is adapted and those in which it should not be used. The manner of applying the cast is described. The contraindications for this method are: (1) combined fracture and dislocation of the humeral head; (2) complete avulsion of the tuberosity; (3) fracture of the neck, with rotation of the head; (4) open fractures, and (5) fractures with interposition of the soft parts between the bone fragments.

Laurence [887] stresses his dislike for traction and casts in treatment of fractures of the humerus and recommends the use of intramedullary Kirschner wires. The results of this treatment in 6 cases were excellent.

Debeyre and Rene [888] treated 2 patients with fracture of the surgical neck of the humerus by inserting a long Smith-Petersen nail through the top of the head of the humerus. In each case, the nail was removed two months after insertion and good functional results were noted.

Bloom [889] has similarly utilized multiple Kirschner wires to immobilize fractures near the head of the humerus. With the arm in midposition, the head of the humerus is anchored by forcing a removable Steinmann pin through the acromion and into the head. Then, with roentgenoscopic observation, the distal fragment is manipulated until the fracture is reduced. Kirschner wires are drilled through the anterolateral surface of the distal fragment, up the medullary space and into the head. Two wires are usually sufficient to hold the fragments. The method was used in 4 cases.

Supracondylar Fractures of the Humerus.—Finck [890] reports 9 cases of malunited supracondylar fracture, in which he explored the frac-

886. Paredes, J. J.: Therapy by Means of Hanging Cast: Fracture of Humerus, Amatus **5**:162-172 (Feb.-March) 1946.

887. Laurence, G.: Intramedullary Kirschner Nail in Treatment of Fractures of the Humerus, Rev. d'orthop. **32**:81-87 (Jan.-April) 1946.

888. Debeyre, M., and Rene, J.: Osteosynthesis with Smith-Petersen Pin in Fractures of the Surgical Neck of the Humerus, Rev. d'orthop. **32**:194-196 (May-Aug.) 1946.

889. Bloom, F. A.: Treatment of Fractures About the Surgical Neck of the Humerus with Closed Reduction and Blind Pinning, M. Rec. **40**:1494-1495 (July) 1946.

890. Finck, C.: Supracondylar Fractures in Children, Torreón méd. **1**:101-120 (May-June) 1946.

ture, excised the callus and new bone, replaced the fragments in normal position and sutured the soft tissues, without any sort of internal fixation.

Sorrel and Longuet [891] describe an anterior incision for exposure of the rare anterior displacement of supracondylar fractures. The authors have used the method in 11 cases and find it valuable in determining the amount of damage to muscles, nerves and blood vessels.

A method of applying traction in bed for patients with supracondylar fractures, known as the Zeno method, is discussed by Riosalido.[892] It consists of the insertion of a Kirschner wire through the olecranon, with application of traction horizontally on the olecranon and vertically on the hand. After a few days to permit reduction of overriding, a band is applied around the upper arm, above the fracture site, and a cast is eventually applied over the traction apparatus when roentgenography shows proper reduction.

[Ed. Note (P. L. N.).—This method of traction is not without danger, as the ulnar nerve may be transfixed during application. Landmarks about the elbow are not easily palpated when the joint is disorganized and badly swollen.]

A series of 47 cases of supracondylar fractures of the humerus in children is reported by LeCocq and Slade.[893] Twenty-five patients were treated by the Dunlop method of traction, with the elbow at an angle of 30 to 40 degrees and with countertraction downward applied just proximal to the elbow. The authors state that gentle manipulation guides the fragments into position when all traction is in place. As a rule complete reduction is shown by roentgenographic check-up in forty-eight to seventy-two hours. One of the main advantages is the avoidance of Volkmann's ischemia, which may result from the classic reduction with the elbow in acute flexion. Traction is maintained for two to three weeks and is then replaced by a plaster mold, with the elbow in flexion at a little more than a right angle. After five weeks a sling is used, and motion is gradually instituted. Of the 25 patients treated by this method, 16 experienced excellent results, with no limitation of movement or residual deformity. Four patients had within 10 degrees of normal motion, and 5 experienced fair results (not within 10 degrees of normal motion).

---

891. Sorrel, E., and Longuet, Y. J.: Anterior Transbrachial Route in Surgery of Supracondylar Fractures in Children, Rev. d'orthop. **32**:117-142 (May-Aug.) 1946.

892. Riosalido, M.: Zeno Traction in Therapy of Supracondylar Fractures, Actas Soc. de cir. de Madrid **5**:187-197 (April-June) 1946.

893. LeCocq, J. F., and Slade, I.: Treatment of Supracondylar Fractures in Childhood, Northwest Med. **45**:30-32 (Jan.) 1946.

[Ed. Note (P. L. N.).—This is a proved and highly satisfactory method of treatment. It is preferable to repeated manipulations.]

A detailed discussion of various types of supracondylar fractures of the humerus, including dicondylar fractures and the T and Y fractures at the distal end of the humerus, is given by Herzog.[894] There is extensive discussion of the clinical and roentgenologic findings, including injuries to the epiphyses and the associated soft parts. The author devotes considerable attention to the prognosis, which so often depends on the timeliness and correctness of the treatment. He discusses the types of fractures in 3 classifications: (1) the cases of slight injury, in which a simple plaster splint is made after correct manual reduction; (2) the cases of severe injury, and (3) the cases of extremely severe damage. In the latter two types, he recommends wire extension on the ulna as the ideal procedure. In addition, there is discussion of other methods of treatments of fractures and of the treatment of residual injuries, such as paralysis of nerves and deformities of the bones, resulting partly from the nature of the fracture and also from improper treatment.

An extensive study of 163 cases of fracture of the lower end of the humerus, in which the patients were treated at the Crown Princess Louise Hospital in Stockholm, is reported by Holmberg.[895] The fractures were classified as "horizontal" (supracondylar or dicondylar) in 142 cases; in 17 cases, the fracture was through the lateral condyle, and in 4, it was through the medial condyle. In 87 of the horizontal fractures, the distal fragment was dislocated backward. Forward dislocation occurred in only 3 cases. A combined dislocation, backward and toward the radius and ulna, often occurred. Rotation between the fragments occurred in 2 cases. The left arm was injured in 61 per cent of the cases. Holmberg concludes that the reason for the poor results in cases in which either a higher degree of varus dislocation or limited mobility remained was the unsatisfactory coaptation of the fragments. Open reduction and fixation with nails is advocated when closed reduction cannot be accomplished.

Injuries to the Elbow.—A roentgenologic analysis of 328 fractures of the elbow, treated at the Centrallasarettet in Borås, Sweden, from 1932 to 1941, is presented by B. A. Nohrman.[896] The follow-up was 80 per cent complete, and the time of observation was two years or more after injury. Sixty-one per cent of the injuries involved the

894. Herzog, H.: Supracondylar Fractures of the Humerus, Helvet. med. acta **11**:615-689 (Nov.) 1944.

895. Holmberg, L.: Fractures of the Distal End of the Humerus in Children, Acta chir. Scandinav. (supp. 103) **92**:1-69, 1945.

896. Nohrman, B. A.: Fracture in the Elbow with Particular Regard to Distal Humerus End, Acta radiol. **27**:409-415, 1946.

distal end of the humerus; 25 per cent, the head and neck of the radius; about 10 per cent, the ulna alone, and 6 per cent, both bones. In 13 per cent of cases, the fracture was combined with luxation. The average age of male patients was 15 years and that of female patients, 25 years. Forty-one per cent of the fractures occurred in adults; these consisted mostly of fractures of the radius and the ulna. The supracondylar fractures were the common injuries in children.

Seventeen cases of injuries resulting from throwing the javelin are reported by Waris.[897] During the first year of competition, the elbow of the throwing arm had in every instance become so painful that the subject was compelled to give up the sport for several weeks to a year. Injury recurred after two to three years. The elbow finally became so insensitive, after repeated injuries, that the subject was able to stand all the strain without pain. The clinical change in the elbow was very slight. Fourteen of 17 subjects showed roentgenologic changes. The majority of these changes were in the tip of the olecranon (in 11 cases). These consisted of different types of fractures in the olecranon and of ruptures of its tips.

Complete fracture of the olecranon, which had healed in a dislocated position, was noted in 3 cases. Rupture of the triangular tip of the olecranon was present in 2 cases, a free calcium shadow at the tip of the olecranon, in 4 and a rough, irregular outline of the tip, in 5.

When the elbow is suddenly straightened during the last stage of throwing the javelin, the tip of the olecranon strikes its fossa and stops the movement of extension. This violent blow is no doubt the cause of the changes in the olecranon. Calcification near the median epicondyle undoubtedly represents the subsequent formation of scars from the ruptures of the medial collateral ligaments and capsules.

The changes in the elbow were all extracapsular after-effects of a definite trauma; no changes resembling those mentioned in Baetzner's theory of arthritis deformans could be found.

[Ed. Note (W. G. S.).—This is an interesting type of athletic injury, which occurs also in the elbows of baseball pitchers, as described by Dr. George Bennett, in 1945.]

Woods[898] describes a case of the extremely rare forward dislocation of the elbow in a sailor of 32 "in a state of alcoholic felicity." Roentgenograms revealed that there was no fracture and that the bones of the forearm were entirely anterior to the lower end of the humerus. Very strong traction was needed to overcome the dislocation, and after

897. Waris, W.: Elbow Injuries of Javelin Throwers, Acta chir. Scandinav. **93**:563-575, 1946.

898. Woods, R. S.: Complete Forward Dislocation of the Elbow, Clin. J. **75**:216-218 (Nov.-Dec.) 1946.

reduction was completed there was pronounced extravasation of blood in the soft tissues. Consequently, light massage and early motion were advised.

The treatment of "sideswipe fractures" (multiple fractures involving the left elbow, the result of the arm's projecting beyond the door of a car when it is sideswiped) is described by Highsmith and Phalen.[899] These fractures are difficult to treat because of the severe trauma to soft tissues; poor results are likely. Amputation may be necessary through the site of the humeral fracture when circulatory damage is pronounced. Débridement, approximation of fragments, immobilization and, later, if necessary, grafting of bone was the order of procedure in 7 cases.

An extensive article on resection of bone fragments in comminuted infected fractures of the elbow is presented by Nicholson.[900] A group of patients treated early in the campaign in the Solomon Islands by resection of fragments three to ten days after injury did very well. No follow-up was possible because of evacuation of the group. Later, 12 other patients with compound fractures involving the elbow joint, caused by bullet or shrapnel wounds, were operated on from two to six months after injury, and fragments were removed. Draining wounds existed at the time of operation in 11 of these cases. The cases were followed from one to seventeen months. There were no major complications after resection of fragments. The patients were allowed up with a sling on the second day after operation, and elbow motion was begun two weeks after operation. Primary closure of infected wounds was done when penicillin was available. Healing time of the wounds depended on the extent of soft tissue damage. Functional results were best when there was little loss of bone substance. In cases with preservation of the trochlear surfaces of the humerus and ulna, the elbow joint, to all intents and purposes, functioned normally. With loss of the olecranon or the condyle of the humerus the power of extension was sacrificed. The loss of trochlear surface in the ulna produced lateral instability in relaxation and a slight loss of power of flexion. Lateral instability of more than 45 degrees resulted in loss of the ability to abduct the extended arm. Resection of 2 or 3 inches (5 or 7.5 cm.) of the humerus resulted in a longer period before power of flexion was regained and in the least stable joints. The widest resection possible was considered to be 3 inches. The ability actively to supinate and pronate the forearm was

899. Highsmith, L. S., and Phalen, G. S.: Sideswipe Fractures, Arch. Surg. **52**:513-522 (May) 1946.

900. Nicholson, J. T.: Compound, Comminuted Fractures Involving the Elbow Joint: Treatment by Resection of Fragments, J. Bone & Joint Surg. **28**:565-575 (July) 1946.

with 1 exception dependent on the absence of the radial head. Function was improved in 3 cases by secondary removal of the radial head. The only patient with supination deformity had not had the radial head removed. In all cases, pronation was more difficult to obtain than supination. A joint space did not redevelop at the site of the resected elbow, but fibrous scar tissue persisted between the bone ends six months after operation. Formation of bone spicules was observed but had not resulted in loss of function.

The results in 21 consecutive cases of fracture of the epiphysis of the medial epicondyle of the humerus, with displacement into the elbow joint, are reviewed by Smith [901] from the fracture service of the Presbyterian Hospital in New York. The ages of the 21 patients were from 7 to 17; 18 were from 9 to 14. Treatment was surgical with exposure of the joint, extraction of the medial epicondyle from the joint, reduction of the dislocation of the elbow and, finally, fixation of the epicondyle to the condylar ridge by means of a heavy silk suture passed through a drilled hole in the ridge. This procedure was used in 15 cases; in 1, a stainless steel screw was used, and in 5, the epicondyle was excised and the conjoined tendon of the flexor pronator group of muscles was sutured to the medial condyle with heavy silk. Follow-up reports in 20 of the 21 cases are given. These averaged three years. Results in 6 cases were perfect; in 4, excellent results were noted (slight prominence or irregularity of the medial epicondyle); in 9, results were good to excellent (slight limitation of elbow flexion or extension), and in 1 case, the result was fair, the epicondyle having been removed after a previous operation in another clinic. No economic loss occurred in any case. All patients with ulnar palsy recovered complete function.

In a discussion of fractures of the olecranon, Wertheimer [902] maintains that closed reduction is satisfactory only when there is no separation between the fragments and they are in perfect apposition. He lists indications for surgical treatment, illustrating treatment with steel wire, graft, nails and sutures. He presents 15 cases, treatment in 11 of which was by open operation. In 6 of these, cotton thread was used; in 1, heavy silk; in 2, nails, and in 1, a Moreira screw.

Hustin [903] reports 12 cases of fracture of the olecranon, in which he treated the fracture with the Davis lag screw. With a special screw driver and by marking the point of entrance for the screw, it was

901. Smith, F. M.: Displacement of Medial Epicondyle into Elbow Joint, Ann. Surg. **124**:410-425 (Aug.) 1946.

902. Wertheimer, L. G.: Fracture of Olecranon, Rev. clín. de São Paulo **18**:87-92 (Sept.) 1945.

903. Hustin, A.: Suture of Fractures of the Olecranon with Screws, Mém. Acad. de chir. **72**:261-262 (April 10-May 15) 1946.

possible to place this deep-threaded screw in the center of the cancellous bone of the ulna.

Key [904] presents the case of a boy of 11, seen forty-eight hours after injury, with the head of the radius displaced into the posterior part of the joint. The head was removed through a posterolateral incision and then was replaced in approximately normal position, the elbow was fixed to 90 degrees and the soft tissues were sutured around the head. The arm was immobilized for eight weeks. Thirteen months later movement of the elbow was almost normal, with 5 degrees less extension than on the other side. There was no pain and growth was satisfactory, although late roentgenograms showed an irregularity of the epiphysial plate.

Fractures of the Forearm.—An excellent article including the study of supination and pronation, with special reference to treatment of forearm fractures, is presented by Patrick.[905] The study is based on 637 cases of fractures of the forearm, from which are excluded those with imperfect reduction or malalinement. The author discusses limitation of rotation following union without displacement. He states that limitation of rotation develops in Colles' fractures, persisting for many months and sometimes becoming permanent. Patients with this type of fracture experience pain over the head of the ulna, in connection with forced supination or pronation. Most fractures of the head of the radius produce no limitation of rotation unless there is comminution or pronounced displacement, necessitating operation.

Patrick states that, since the normal range of pronation is checked by the radius crossing the ulna and compressing the deep flexor muscles between the two bones, anything encroaching on this space, such as fibrous tissue, callus or edematous tissue, will alter the compressibility of the flexor muscles and limit pronation. In all fractures of the middle third of the radius or ulna some loss of pronation occurs and persists for a considerable time after union has taken place. In isolated fractures of the ulna some degree of loss of rotation is present for a time after union, especially in fractures at the level of the attachment of the interosseous membrane. Fibrous tissue or callus rarely extends far enough to involve the radius. In isolated fractures of the radius operation causes some increase in fibrous tissue reaction around the fracture, but any further involvement of the interosseus membrane from the radial side does not affect the range of rotation.

Fractures of the shaft of the radius and ulna above the level of the interosseous membrane are rare; there are only 7 in this series,

904. Key, J.: Survival of Head of Radius in Child After Removal and Replacement, J. Bone & Joint Surg. **28**:148-149 (Jan.) 1946.

905. Patrick, J.: Study of Supination and Pronation with Special Reference to Treatment of Forearm Fractures, J. Bone & Joint Surg. **28**:737-748 (Oct.) 1946.

in all of which union took place with minimum displacement and no loss of supination or pronation occurred once the fractures had united.

In fractures of both the radius and the ulna, limitation of rotation is due to a combination of the factors present in fractures of the radius and ulna occurring separately. The triangular fibrocartilage often escapes damage in double fractures of the forearm, so that the fractured ulna is the main cause of limitation of rotation.

Zarazoga [906] analyzes a series of 279 cases of fractures of the forearm in children. In the age group from 3 to 5, only the middle third of the forearm was involved. In children from 6 to 10, the fractures occurred in the middle and lower thirds of the arm, and at 12, in the middle third again. In 80 per cent the cause was indirect violence; 12 per cent of these fractures were complicated. In 20 per cent the cause was direct, one-half of these fractures being compound. Fractures of both bones occurred in 75 per cent of patients, and isolated fractures of the radius occurred in 20 per cent. Fractures of the ulna occurred in only 5 per cent, fracture of the ulna with luxation of the radius, in 3 per cent, and fracture of the radius with luxation of the ulna, in slightly less than 3 per cent. The author states that loss of rotation rarely develops in children when a reasonably good closed reduction of the fracture has been obtained.

Fractures of the forearm are discussed by Agrifoglio,[907] with the recommendation of the following procedure if ordinary methods of reduction should fail: manual traction for two to five minutes; reduction by pressure with the fingers, and fixation with a plaster splint, holding the forearm in pronation and the hand in pronation and dorsiflexion. Open reduction is recommended if this procedure also should fail. The author suggests using a splinter of bone from the fracture site as an intramedullary peg to hold the fragments in place and tying the fragments together with heavy catgut. Immobilization is maintained for at least six weeks. Excellent results were obtained in 5 cases.

Caceres [908] presents 2 cases of fracture of the bones of the forearm in young children (5 and 9), in which he used a simple expedient for reduction and retention. In the case of the child of 9, there was a fresh fracture of the radius, two fingerbreadths above the styloid apophysis. In the second case, both bones were fractured higher. The method used by the author was insertion of a Steinmann pin from the dorsal surface through the radius, using it as a lever to assist in the

906. Zarazoga, J.: Forearm Fractures in Children, Rev. méd. de Córdoba **34**:75-82 (Feb.) 1946.

907. Agrifoglio, M.: Bloodless Therapy and Intramedullary Pegging in Fractures of Lower Segment in Adolescents, Arch. ortop. **57**:60-72 (Jan.) 1942.

908. Caceres, M. A.: Treatment of Forearm Fractures Difficult to Reduce and Maintain in Position, Semana méd. **1**:248-253 (Feb. 7) 1946.

reduction of the fracture, after which a plaster cast was applied directly to the skin, with reenforcement around the pin to prevent its moving. In both cases, reduction was excellent and consolidation prompt, with perfect functional and esthetic results. The use of metallic osteosynthesis on growing bones is usually dangerous, but the author considers the procedure to be without risk. The approach is from the dorsum, to avoid important vessels and nerves.

[Ed. Note (W. G. S.).—This procedure is much like the pin fixation in cast which was described by J. E. M. Thomson many years ago.]

Rose [909] describes a simple but effective device for applying traction to the wrist and forearm. It consists of two crossbars, which clamp to the table top and project about 12 inches (30 cm.) over the side. The patient's head lies on the upper one, with the upper arm parallel to the bar and about 4 inches (10 cm.) from it. The arm is attached to the bar with a band of gauze. A felt pad on the anterior aspect of the arm is for countertraction. The elbow is then bent to 90 degrees, and traction is applied to the forearm with a single loop of 3 inch (7.5 cm.) gauze bandage around the thumb. The gauze is tied to sash cord passed through a pulley attached to the lower bar, which is at the patient's feet. Two weights, up to 25 pounds (11.3 Kg.) each, are applied for thirty minutes. The device has been used by eighty to ninety surgeons at Charity Hospital in New Orleans in the reduction of over 1,500 fractures of the forearm, without a single instance of circulatory complications. The cast can be applied with the traction device in place. Traction can also be applied to the middle finger instead of to the thumb, for traction in the line of the axis of both bases. For reduction in cases of Colles' fracture, the thumb is used.

Maia [910] reports a group of 8 cases of Monteggia's fracture, 6 of which were in children and 2, in adults. There was one open reduction. Good results were reported in all cases. The author states the belief that open operation should be reserved for old fractures and those with involvement of the nerves.

Two cases of nonunion after the use of Kirschner pins in both bones of the forearm are reported by Guilleminet.[911] One was in a boy of 7. The pins were put in the day after the fracture occurred and removed in twenty-five days. The arm was kept in plaster. Three months later, there was angular deformity. The bone ends were freshened and the pins reinserted and left in for three months.

---

909. Rose, R. M.: Simple Traction Device for Reduction of Forearm, J. Bone & Joint Surg. **28**:176-177 (Jan.) 1946.

910. Maia, B.: Monteggia Fracture, Arq. brasil. de cir. ortop. **12**:181-188, 1944.

911. Guilleminet, M.: Intramedullary Nailing of Both Bones of Forearm, Lyon chir. **40**:763-765 (Nov.-Dec.) 1945.

Fractures of the Wrist.—An analysis of 66 cases of fractures of the carpal scaphoid bone is presented by Bannerman.[912] In this series of cases, 42 per cent of the fractures of the carpal scaphoid bones were not diagnosed at the time of injury. In 35 per cent of the series, the fractures were either diagnosed as sprains and not examined roentgenographically or the roentgenogram was reported as not showing fracture and the diagnosis was missed. These factors resulted in prolonged convalescence. Complete and prolonged immobilization is the accepted treatment in all cases, even ten months after injury; satisfactory results were observed in 15 per cent more of the patients who received this treatment alone. Reduction of fractures of the carpal scaphoid bone is seldom necessary. When seen in association with dislocation of the semilunar bone, the fragments of the carpal scaphoid bone are usually in a good position after the semilunar bone has been reduced. The series contains 2 cases of this type. Immobilization by skin-tight cast, involving the thumb and extending from the elbow to the distal palmar crease, was the method used. The wrist was held in moderate dorsiflexion and slight radial deviation. The thumb was held in abduction, and extension was included to the distal phalanx. The cast was changed when it became loose, owing to atrophy of the muscles of the forearm. The atrophy was minimized by use of the fingers during immobilization. Roentgenograms taken in all positions every six weeks, and immobilization was continued until the fracture line disappeared. Inclusion of the thumb is essential for the purpose of holding the fragments in most intimate contact, and because complete immobilization cannot be accomplished unless this is done; union rarely occurs when the thumb is not included.

In 56 cases, or 85 per cent of the series, the fracture was healed without arthritic changes by prolonged immobilization. The presence of osteoporosis of the carpal scaphoid bone due to trauma was no bar to healing in the 6 cases of this condition. Immobilization was continued until complete revascularization had taken place. This was evidenced by the gradual decrease of sclerosis of the fragment and by the restoration of uniform density, as shown in roentgenograms.

Operation was not done until at least two months of immobilization had failed to show improvement. Operation was performed in 10 cases; fractures in 6 of these healed, with good results. In 2 cases with pronounced arthritic change, the distal fragment was removed; the result was good in 1. After immobilization recovery of function was surprisingly rapid in both operative and nonoperative cases. All patients regained full motion and strength after only one month of use and physical therapy.

912. Bannerman, M. M.: Sixty-Six Cases of Fracture of the Carpal Scaphoid, Arch. Surg. **53**:164-168 (Aug.) 1946.

Fracture of the carpal scaphoid is common in military practice, and from the standpoint of time lost, persistence of symptoms and disability, the condition is comparable to fracture of the femoral neck. Disability is due to failure to recognize the fracture soon after injury, to inadequate treatment (with regard to immobilization during the period of fixation) or to disturbance of circulation to the proximal fragment, with delay in union. Sashin [913] saw 64 patients with such fractures from January 1943 to April 1945. Only 39 patients had undergone immobilization of the wrist in plaster soon after injury; in this group, 34 had union. Nonunion was found in 29 of the 64; 20 were operated on (methods consisted of excision of the proximal fragment or drilling or grafting of bone). Firm bony union was obtained in 4 cases; in 4 others, there was roentgenographic evidence of union, but the fracture line was visible six months after operation. In 2, there was no union after grafting of bone, so excision of the proximal fragment was done.

A lengthy, detailed roentgenographic study of the carpal scaphoid is given by Trial,[914] who presents a table of six positions to be used in taking roentgenograms of this fracture. The author discusses the types of fracture occurring in the scaphoid and recommends that these roentgenographic views be taken: (1) anteroposterior view with fist closed; (2) anteroposterior view with the palm to the plate; (3) front views of both hands in moderate abduction and (4) a lateral and two oblique views.

[Ed. Note (W. G. S.).—In questionable cases these special views would be of great value.]

Bedrick and Zawadzki [915] emphasize that wrist injuries are rarely simple sprains and should be studied at roentgenologic examination. Fracture of the scaphoid is shown more easily by ulnar deviation of the hand than by radial deviation or anteroposterior projection. The diagnosis is usually based on the history of a fall on an outstretched hand, and the treatment for a fresh fracture is immobilization in an unpadded plaster cast for eight weeks. In doubtful cases, the injury should be treated as a fracture and roentgenograms made again in ten days. The authors state that old fractures were treated either with a bone peg or by simple drilling through and across the fracture line. The authors saw 31 fractures of the carpal scaphoid among 210 fractures of the forearm and wrist observed in thirty-six months. Bony

913. Sashin, D.: Treatment of Fractures of the Carpal Scaphoid: Report of Sixty-Four Cases, Arch. Surg. **52**:445-465 (April) 1946.

914. Trial, R.: Roentgen Exploration of Carpal Scaphoid and Its Application to Diagnosis of Fractures, Rev. corps san. mil. **1**:504-526, 1945.

915. Bedrick, J. J., and Zawadzki, S. A.: Some Observations on the Fractured Carpal Scaphoid, Mil. Surgeon **98**:488-491 (June) 1946.

union occurred in 95 per cent of the cases of fresh fracture treated by immobilization in a skin-tight cast.

Macrossan [916] presents reports of 3 cases of sprain, with and without "flake" fracture of the carpal scaphoid, in boys of 11 and 12. The sprains occurred at the attachment of the radial collateral ligament of the wrist joint to the scaphoid. The violence producing them was forcible ulnar deviation, accompanied by palmar flexion or dorsiflexion at the wrist. The maximal point of tenderness was in front, over the tuberosity of the scaphoid, in what appeared to be a minor strain of the wrist. Roentgenograms may show partial separation of a discrete flake of bone or evidence of a lesser degree of damage to the scaphoid at the attachment of the radial collateral ligament. Fixation in plaster is necessary when symptoms persist beyond a week or two.

Fractures of the Hand.—Acute injuries of the first metacarpal bone in military personnel are discussed by Van Demark.[917] In cases of Bennett's fracture combined with dislocation of the thumb, when manipulative reduction is not successful, the treatment of choice is skeletal traction, applied through the distal part of the first metacarpal bone or the proximal phalanx and combined with immobilization in plaster of paris in the position of function. The cast should cover the forearm and be closely molded laterally at the base of the thumb, and in the palm it should extend to the level of the necks of the metacarpal bones, permitting full motion of the fingers. Fracture of the shaft and base of the first metacarpal bone usually occurs at or near the junction of the shaft with the base. The distal fragment is angulated medially by the thenar and the long flexor muscles of the thumb, the proximal fragment being held in abducted position by the long abductor muscle. After reduction and immobilization in plaster frequent roentgenologic examination is done. With proper care an almost perfect anatomic result can be obtained. A similar brief discussion of sprains and subluxations of the adjacent joints and of dislocation of the first metacarpophalangeal joint is included in this report. In cases of dislocation of the first metacarpophalangeal joint, closed reduction is usually possible and should be followed with a four week period of immobilization in flexion, to prevent recurrence.

Twenty cases of fractures of the shaft of the metacarpal bones were treated by Barba Inclán [918] after the method of Berkman and Miller, in which one or two Kirschner pins are introduced from the side of

916. Macrossan, K. I.: Sprain Fracture of the Carpal Scaphoid in Children, Lancet **1**:341-342 (March) 1946.

917. Van Demark, R. E.: Acute Injuries of First Metacarpal in Military Personnel, Mil. Surgeon **99**:127-130 (Aug.) 1946.

918. Barba Inclán, A.: Internal Fixation in Therapy of Fractures of the Last Four Metacarpals, Bol. Sec. san. policia nac. **1**:62-65 (April-June) 1945.

the hand nearest the fractured metacarpal bone. The first metacarpal bone is excluded from this treatment, and the author also makes an exception in cases of avulsion of the styloid process of the third metacarpal bone, for which he recommends open operation and direct suture.

The mechanism of metacarpophalangeal luxations of the thumb is discussed in an article by Giordanengo.[919] The author describes three types of luxation and discusses the differential diagnosis of this condition when it is complicated by fracture of the distal end of the metacarpal bone or the proximal end of the phalange. Maneuvers for reduction are described.

The treatment of fracture-dislocation of the interphalangeal joints of the hand is discussed by Robertson and Cawley.[920] The injury occurred in 7 cases recorded in a large Army general hospital in one year, as a result of baseball injuries. The injury was due to a blow on the end of an extended finger, which produced a small, palmar fragment, retracted proximally by the capsule. Treatment was with three Kirschner wires connected to a wire extension, the first transversely through the neck of the proximal phalanx, the second transversely through the base of the phalanx distal to the dislocation and the third transversely through the neck of the phalanx. With rubber bands, traction was obtained on these wires to reduce and hold the fracture. In all 7 cases, reduction was well maintained, bony union of the fragment was obtained and function was excellent.

Curry [921] stresses the importance of painstaking care in industrial injuries of the fingers. Roentgenologic examination of all suspected fractures, before and after reduction, is important. The author outlines the methods of treatment for fractures involving the distal phalanx, the middle phalanx, the proximal phalanx and the thumb, indicating the insertions of tendons which produce different deformities and the type of flexion or extension which will overcome such deformities. The underlying principle in treatment of all fractures of the finger is the matching of the mobile distal segment to the less mobile proximal segment. Disturbance of the circulation must be prevented. In the section on amputations the author emphasizes the importance of saving as much of the finger as possible, as reparative processes are complicated. The loss of soft parts, continuous pain from permanently damaged nerves, complete loss of tendons and fixation of a joint, with

919. Giordanengo, G.: Dislocations of the Metacarpophalangeal Luxations of the Thumb, Minerva chir. **1**:92-94 (May) 1946.

920. Robertson, R. C.; Cawley, J. J., Jr., and Faris, A. M.: Treatment of Fracture Dislocation of Interphalangeal Joints of Hand, J. Bone & Joint Surg. **28**:68-70 (Jan.) 1946.

921. Curry, G. J.: Treatment of Simple and Compound Finger Fractures, Am. J. Surg. **71**:80-83 (Jan.) 1946.

deformity, are among the indications for amputation. Sites that are best for amputation are listed.

A method of reducing fracture-dislocations of the proximal interphalangeal joints of the fingers is described by Schulze.[922] The procedure consists of placing the joint in extreme flexion while producing traction on the finger, thus reducing both the fracture and the subluxation. In most cases, no pressure is required to maintain reduction as long as the position of acute flexion is not allowed to lapse. The position can be maintained with a strip of adhesive tape placed around the flexed finger. If the finger is short and thick or if swelling interferes with full flexion it may be desirable to use a splint made of a strip of aluminum. Because of the pain and the immediate, pronounced deformity, these injuries are usually seen early, at which time swelling is generally not great and reduction is accomplished with little pain. In a week or ten days, the finger is gradually extended, while immobilization of the joint and protective splinting are continued.

FRACTURES OF THE LOWER EXTREMITY

Fractures and Dislocations About the Hip Joint.—Feldman[923] states that gunshot wounds of the hip were the gravest injuries of the extremities observed during the war. These wounds were often accompanied with severe complications, giving rise to high mortality and to invalidism. Sepsis with anaerobic infection was the main cause of death among patients returned to hospitals in the rear. The author states the belief that results depend fundamentally on the length of time before removal from the battlefield, on the quality and time of surgical treatment and on immobilization. He recommends careful surgical treatment under complete anesthesia and advises immediate amputation when virulent gaseous infection is present. The need to prevent complications by cleanliness of the wound, careful surgical treatment, blood transfusions and massive intravenous doses of sulfanilamide is stressed. The author recommends concentration in one army hospital of all patients with grave injuries to the extremities, particularly those with hip injuries.

Alcivar-Elizalde[924] discusses 2 cases of fracture of the femoral shaft with dislocation of the hip in the newborn, caused by forcible maneuvers during delivery. The clinical picture in each case was characteristic, showing disproportion in the length of the infant's limbs, with pain

922. Schulze, H. A.: Treatment of Fracture-Dislocations of Proximal Interphalangeal Joints of Fingers, Mil. Surgeon **99**:190-191 (Sept.) 1946.

923. Feldman, K. I.: Therapy of Gunshot Wounds of Hip, Khirurgiya, 1945, no. 3, pp. 55-63.

924. Alcivar-Elizalde, E.: Obstetric Dislocation of Hip Associated with Fracture of Femur, J. Bone & Joint Surg. **28**:838-841 (Oct.) 1946.

on motion, followed in two to three days by swelling in the inguinal, thigh and gluteal regions. The prognosis was favorable when treatment was started during the first fifteen days after birth. The author used the Lorenz procedure, employed for congenital dislocations, and ether anesthesia. The normal hip was fixed while the operator flexed the injured thigh on the abdomen, with the hip and knee flexed. The extremity was then rotated externally. This maneuver was sufficient to produce reduction, which was checked by roentgenograms. Immobilization, with the limb in 135 degrees flexion, 40 degrees abduction and slight internal rotation, was maintained for forty-five days in a castex• or plaster spica. The results in these 2 cases were good, as shown by roentgenograms and by the efficiency of the limb, the infants having learned to walk at 14 or 15 months, with normal gait and development.

[ED. NOTE (W. G. S.).—These injuries were complete dislocations with incomplete fractures, which explains the author's success with manipulative reduction.]

Quist-Hansen [925] reports that 10 traumatic dislocations of the hip joint comprised 8.5 per cent of all dislocations observed at the Municipal Hospital in Bergen, Norway, during the period from 1927 to 1941. He states that laceration of the ligamentum teres and lesion of the capsule in a traumatic dislocation lead to a greater risk of ischemia of the femoral head in children and adolescents than is the case in full-grown persons. The author presents a case of necrosis of the femoral head, the condition having occurred after traumatic dislocation of the hip joint in a boy of 4. The patient was observed for a period of two and a half years. A control examination of 8 other patients with traumatic dislocation of the hip joint, of which 3 were under 10, revealed no signs or symptoms of necrosis of the head two and three quarters to ten and a half years after injury. The author recalls that experiments on animals by Muller, in 1924, demonstrated the high frequency of necrosis during the period of growth. A comparison of age distribution in 370 cases of traumatic dislocation of the hip joint and in 49 cases of necrosis of the femoral head after this injury shows that in human beings the risk of necrosis of the head is great during the period of growth, with a rapid drop in frequency after the closing of the epiphysial line at the age of 18 to 20.

Sabate [926] gives a detailed case history of a man of 20, who at the age of 13 had experienced an ischiatic type of coxofemoral dislocation due to a fall; the dislocation was reduced, and the hip functioned

925. Quist-Hansen, S.: Caput Necrosis After Traumatic Dislocation of the Hip Joint in Four Year Old Boy: Control Examinations of Eight Cases of Luxatio Coxae Traumatica, Acta chir. Scandinav. **92**:393-402, 1945.

926. Sabate, S. J.: Necrosis of the Head of the Femur Following Ischiatic Variety of Coxo-Femoral Luxation, Med. clin., Barcelona **6**:171-176 (March) 1946.

normally for seven months. A second fall then produced pain in the hip, which was violently manipulated once weekly for a month, after which reluxation of the femoral head was followed by claudication and pain, which lasted for months. There was gradual improvement, and when the author again saw the patient at the age of 20, there was little outward evidence of the condition of the hip. The author includes a lengthy analysis of the pathologic conditions in this case of aseptic necrosis, followed by a lengthly discussion of the causes and measures for preventing such disturbances.

Intertrochanteric Fractures.—O'Brien, Shy and Bublis [927] report on 103 consecutive cases in which trochanteric fractures were treated by internal fixation. Spinal anesthesia was used in 29 cases, with 4 deaths (13.8 per cent); ether drop method in 10, with 2 deaths (20 per cent); thiopental sodium (pentothal sodium®) and nitrous oxide anesthesia in 34, with 3 deaths (8.8 per cent), and local anesthesia in 30, with 13 deaths (43.4 per cent), a total of 22 deaths (21.4 per cent) from anesthesia. The average age of the patients was 70.6, including persons up to 89. The operative technic for reduction and insertion of the blade plate is described in detail, as is the postoperative care. The result of a one to two and a half year follow-up of 50 of the 81 survivors were: 20 (40 per cent), excellent; 11 (22 per cent), good; 8 (16 per cent), fair, and 11 (22 per cent), poor.

Briggs and Keats [928] recommend skeletal traction with beaded Kirschner wires for treating intertrochanteric fractures of the femur. The authors consider the advantages of this method to be ease in nursing care, early mobilization of the knee and almost perfect anatomic reduction; they treated 18 of 32 patients in this way, with good functional and excellent anatomic results in 16. The method of application is described.

Fractures of the Neck of the Femur.—Numerous articles were published on this subject in 1946, but no radical changes or new ideas were presented.

Menegaux and Lescaux [929] illustrate the current trend away from the use of guides. Theirs is an illustrative comment that the numbers of new directional guides presented yearly for nailing fractures of the femur would make one think that this operation has only one

927. O'Brien, R. M.; Shy, J. C., and Bublis, N. J.: Internal Fixation of Trochanteric Fractures of Femur: Report of One Hundred and Three Consecutive Cases, J. Bone & Joint Surg. **28**:791-797 (Oct.) 1946.

928. Briggs, H., and Keats, S.: Management of Intertrochanteric Fractures of the Femur by Skeletal Traction with Beaded Kirschner Wire, Am. J. Surg. **71**:788-796 (June) 1946.

929. Menegaux, G., and Lescaux, B.: Nailing of Fractures of the Femoral Neck Without Directional Apparatus, Mém. Acad. de chir. **71**:368-373 (Oct. 17-31) 1945.

delicate stage (the placing of the guide) which is all-important to the success of the nailing. The authors dispensed with the guide in the last 17 of the 50 cases reported; the importance of perfect reduction with adequate roentgenographic control is stressed as being of more significance than the use of guides for aiming a nail.

Chaton [930] also recommends simplification of the technic for nailing of fractures of this type and suggests preliminary reduction and immobilization in plaster before moving the patient to the operating room, where operation is performed through a windowed cast.

[ED. NOTE (W. G. S.).—This method would perhaps simplify the technic in small hospitals where no fracture table is available, but otherwise it would seem to be superfluous.]

Pelissier [931] presents his aiming apparatus, which is an adaptation combining the best features of the Bopp goniograph and the Merle d'Aubigne apparatus.

DoAmaral [932] presents a lengthy thesis, with a detailed anatomic study, classification of fractures and a discussion of relative frequency, symptoms, roentgenographic diagnosis and treatment. He reviews 9 cases in which fractures were treated by Whitman reduction; 5, with the Albee bone peg; 6, with Smith-Petersen nailings and 24, with the Godoy Morlira screw. He reported osseous union in 21 and pseudarthrosis in 3 cases in the last group.

Speed [933] lists the errors of omission and of commission usually responsible for failure in the surgical treatment of fractures of the hip and stresses the need for frequent roentgenologic checking during and after fixation, for the proper angle of insertion of nails or pins, for proper support for the fracture and the avoidance of too early weight bearing. The author considers bone grafts in addition to nails or pins to be of insufficient value for the added trouble and time required. For nonunion he recommends subtrochanteric osteotomy as giving better results than attempts at reduction and pin fixation.

Barba Inclán [934] describes his method of treatment in stages. The first is reduction under local anesthesia, with insertion of a Stader

930. Chaton, M.: Attempted Simplification of Technic of Nailing Fractures of the Femoral Neck, Mém. Acad. de chir. **71**:488-491 (Nov. 28-Dec. 19) 1945.

931. Pelissier, G.: The Purpose of Nailing of Fractures of the Femoral Neck: Presentation of an Aiming Apparatus, J. de radiol. et d'electrol. **27**:255-256, 1946.

932. doAmaral, A. C.: Therapy of Fractures of the Femur by Brazilian Method of Godoy Moreira (Extra-Articular Fixation), Rev. méd. munic. **6**:245-295 (March-April); 478-532 (May-June) 1946.

933. Speed, K.: Treatment of Fractures of the Hip: Surgical Technic, S. Clin. North America **26**:230-248 (Feb.) 1946.

934. Barba Inclán, A. B.: Surgical Therapy of Fractures of the Neck of the Femur by Bone Graft in Several Stages, Cir. ortop. y traumatol., Habana **12**:106-114 (July-Sept.) 1945.

nail in the lower third of the femur for maintenance of the position in a plaster spica. The second stage, which is carried out one week after the reduction, is removal of a cortical graft from the tibia of either the patient or a bone donor. The graft is kept in citrated blood, under refrigeration, for one week. The third stage, performed after another week, consists of insertion of the bone graft. A large window is cut in the spica over the trochanteric region, and with the aid of the author's guide and a roentgenographic check the previously modeled graft is inserted in a drilled hole. Use of the spica is continued after operation for seventy to eighty days, and walking with crutches is begun in one hundred days.

Therkelsen [935] describes an extracapsular method for removal of the central fragment of a broken steel nail: A thread is cut in the central fragment and a screw inserted, which can be used as a handle for removal.

Joensen [936] and Branes [937] each report a case of spontaneous fracture of the femoral neck following roentgen irradiation and radium therapy for cancer of the cervix. Both fractures occurred two years after roentgen therapy was first given. Joensen collected from the literature reports of 25 cases of spontaneous fracture of the femoral neck following roentgen irradiation; the fractures were bilateral in 2 cases. In 1 case ankylosis of the hip resulted from irradiation without evidence of a fracture.

Pennis,[938] in a study of the end-results of fractures of the femoral neck, reports on 254 cases from the files of the state insurance fund of the Netherlands. Most of the patients were men, the exact number being 228 men and 26 women. The average age was 49.7; only 4 patients were over 69, and 12 were under 40. The results were good in 163 cases, satisfactory in 18, unsatisfactory in 56 and unknown or questionable in 17; results were thus good or satisfactory in nearly 70 per cent of the cases. The data on type of therapy are vague, which is not surprising in view of the source of the material and the author's purpose in studying this particular type of statistics.

---

935. Therkelsen, F.: Extracapsular Removal of Broken Steel Nail Used in Osteosynthesis of Femoral Neck, Nord. med. (Hospitalstid.) **15**:2301-2302 (Aug. 15) 1942.

936. Joensen, H. D.: Spontaneous Fracture of the Femoral Neck Following Roentgen Irradiation, Nord med. (Hospitalstid.) **12**:3718-3720 (Dec.) 1941.

937. Branes, J. F.: Fractures of the Femoral Neck Following Roentgen and Radium Therapy of Cancer of the Uterine Cervix: Case, Arch. Soc. cirujanos hosp. **15**:589-591 (June) 1945.

938. Pennis, P. W. L.: Therapeutic Results of Fractures of the Femoral Neck According to Data of State Insurance Fund, Nederl. tijdschr. v. geneesk. **90**:147-149 (Feb. 16-22) 1946.

[Ed. Note (W. G. S.).—Obviously a series of cases in this group of young persons, composed mostly of men, would yield a higher percentage of satisfactory results than is usually reported. However, I feel that the author's outlook is a little optimistic, even considering the unusual source of material.]

Leira [939] reports the end-results in 103 cases of fracture of the femoral neck, observed from 1933 to 1941 in the Trondheim Hospital in Norway. Thirty-nine patients were treated by traction, reduction or bed rest, or with plaster casts; 64 were treated with the Smith-Petersen-Johansson nail. The minimum period of observation was two years. In both groups women predominated; results were far better in the case of men. In the nonsurgically treated group more than half the patients showed displacement of the fracture site and 6 had necrosis of the head of the femur. Two failures were considered due to initial trauma, 2 secondary to pseudarthrosis and 2 secondary to early weight bearing. In the surgically treated group, in which 64 fractures were nailed, satisfactory results were recorded in 32 cases, good results in 2 and unsatisfactory results in 30; osseous union occurred in 87.5 per cent. The unsatisfactory results were ascribed to aseptic necrosis in 17 cases, to pseudarthrosis in 8 (12.5 per cent) and to arthritis deformans in 22 (45 per cent). In conclusion, the author states emphatically that the patient should be kept in bed until osseous healing of the fracture occurs.

Harstad and Paulsen [940] studied 112 cases of fractures of the femoral neck treated by nailing. Reexamination was made one to six years after initial treatment; in 84 cases examination was roentgenographic, and in 28 clinical. Results in 60 per cent of the cases were considered satisfactory. Pseudarthrosis was present in 16 cases and aseptic necrosis in 13. Unsatisfactory reduction and unsatisfactory position of the nail were considered the chief causes of pseudarthrosis. Aseptic necrosis seemed to be almost inevitable, since it occurred in cases in which the patients showed good reduction and osseous union. The authors state that the nail is of no importance as a causative agent for aseptic necrosis.

Heide-Jørgensen and Schondel [941] report the cases of 58 patients, 47 with fractures of the femoral neck and 11 with pertrochanteric fracture; 30 were 70 at the time of treatment. All were treated surgically,

939. Leira, H.: Results of Treatment of Fractures of the Femoral Neck in Trondheim Hospital from 1933 to 1941, Nord. med. **31**:2084-2094 (Sept. 13) 1946.

940. Harstad, K., and Paulsen, K.: Examination of Nailed Fractures of the Femoral Neck, Nord. med. (Norsk mag. f. lægevidensk.) **27**:1571-1574 (Aug. 10) 1943.

941. Heide-Jørgensen, H., and Schondel, C.: Surgical Therapy of Fracture of Femoral Neck and of Pertrochanteric Fractures with After-Examination of Operated Patients, Nord. med. (Hospitalstid.) **17**:329-331 (Feb. 27) 1943.

the mortality rate being 10 per cent in the cases of fracture of the femoral neck and 9 per cent in those of pertrochanteric fracture. At the end of one year 33 patients were examined, and the results were summarized as follows: excellent, 26 cases; satisfactory, 4; poor, 2, and no opinion, 1. In 4 cases another operation was performed and the fracture nailed again; removal of the nail was done in 7 cases. Bony union occurred in 29 cases, the outcome was uncertain in 1 and unjudged in another and 2 patients had necrosis of the femoral head.

Fractures of the Shaft of the Femur.—McKeever,[942] on the basis of a study of 47 cases of closed fracture of the femur, in all of which the patient, though originally treated by different army surgeons, ultimately came under the author's care, makes recommendations about the promiscuous use by average surgeons of procedures requiring high skill and special armamentarium. Among the 47 patients, 23 had been treated by some form of suspension; 17 had had open reduction and metallic plate fixation and/or screw fixation (10 primary and 7 secondary), and 7 had had external skeletal fixation. The shortest periods of absolute recumbency were seventy days for external skeletal fixation, seventy-seven for internal fixation and ninety for traction. The longest periods were three hundred and sixty-five days for internal fixation, three hundred and twenty-six for external skeletal fixation and one hundred and ninety-three for traction. The author studied other phases, such as protection, the time required for roentgenographic evidence of bony union, the status of the joints, shortening, muscular atrophy and complications, concluding that the safest method for the average surgeon in the average hospital is traction. Under average circumstances open reduction should be reserved for patients showing well founded evidence of soft tissue interposition after a trial of treatment by traction. The general use of apparatus designed for skeletal fixation and ambulation is likely to delay union and carries a great risk of producing osteomyelitis at the sites of fixation pins.

Lusskin and Hoffman[943] discuss the limitations in the treatment of fractures aboard a hospital ship and recommend plaster spica casts with full and half pin fixations. No follow up of the cases is presented.

Hart[944] comments on stiffness of the knee, which he considers the major complication in cases of fracture of the femur. He discusses in great detail a program for the restoration of function through active, objective, resisted and non-weight-bearing exercises.

---

942. McKeever, F. M.: Treatment of Fractures of Shaft of Femur, Bull. U. S. Army M. Dept. **5**:690-696 (June) 1946.

943. Lusskin, H., and Hoffman, R. R.: Fractures of Shaft of Femur: Early Treatment on Hospital Ship, U. S. Nav. M. Bull. **46**:888-894 (June) 1946.

944. Hart, V. L.: Balanced Suspension and Treatment of Fractures of the Femur, Bull. U. S. Army M. Dept. **5**:57-63 (Jan.) 1946.

Allende and Malvarez [945] present 7 cases of traumatic separation of the lower end of the femur, all in boys 7 to 17. In 1 case there was bilateral separation of the epiphysis, and in another the separation was complicated by a fracture of the shaft of the opposite femur. In 2 cases rupture of the popliteal artery produced gangrene of the foot, requiring amputation; the Gritti type of amputation was done in each case. One patient, seen twenty-three days after injury, was treated by removal of the epiphyseal fragment and ankylosis of the knee in extension. The authors recommend reduction in flexion for twenty days and 90 degree flexion for another twenty days, followed with continuous traction to extend the knee. When the displacement was backward skeletal traction for eight to fifteen days was followed by immobilization in plaster, with the knee extended.

Fractures of the Patella.—Two slightly contradictory reports appeared in 1946 on patellectomy as the treatment for fractures of the patella.

Brooke [946] reports on 54 cases, with a follow-up study in 35, in which all patients had undergone excision of the patella five to fifteen years previously. Nineteen had sustained comminuted fractures and 16 transverse fractures, with varying degrees of separation of the fragments. Twenty-five were male and 10 female patients. The average age at the time of operation was 40. All patients returned to work in three to eight weeks after the operation. There were no osteoarthritic changes in any of those examined. In 27 cases function of the affected limb was normal in every respect; in 10 there was some disability, for varying reasons. The author stresses the use of nonabsorbable suture material, preferably linen, and prevention of insufficiency in the quadriceps.

MacAusland,[947] on the other hand, after reviewing the history of patellectomy, including Brooke's several articles reporting strikingly good results, mentions that the indications for the use of patellectomy in the treatment of fractures are still not clearly defined. He lists the advantages and disadvantages of patellectomy but states the opinion that patellectomy should at present be limited to cases of severely comminuted fresh fracture and of malunion after transverse fracture. He discusses operative technic, postoperative care and regeneration of the patella and gives an analysis of cases and results in 11 of his own 14 cases. Ten of the 11 patients obtained good, functional knees, with

945. Allende, G., and Malvarez, O.: Separation of the Epiphysis of the Lower End of the Femur, Prensa méd. argent. **33**:495-506 (March 8) 1946.

946. Brooke, R.: Fractured Patella: Analysis of Fifty-Four Cases Treated by Excision, Brit. M. J. **1**:231-233 (Feb. 16) 1946.

947. MacAusland, W. R.: Total Excision of Patella for Fracture: Report of Fourteen Cases, Am. J. Surg. **72**:510-516 (Oct.) 1946.

perfect motion of the joint and stability. In 4 cases there was slight atrophy of the quadriceps, with loss of 10 degrees of complete extension, but the patients were asymptomatic. Five patients had normal power and motion. One patient had only 90 degrees of motion, with tenderness at the level of the joint, and the remaining patient, although clinically normal, complained of the inconveniece of going up stairs one step at a time.

Fractures into the Knee Joint.—Vergara [948] reports on 20 cases of fracture of the tibial condyle, recorded in the Instituto Traumotológico, Santiago, Chile. In 13 one tuberosity was fractured, and in 7 both tuberosities. Only 1 case was treated surgically, because of an intra-articular fragment, and although there was good function at first, the residual deformity resulted in 30 per cent disability. The author states that the spongy character of the condyle is a contraindication for surgical repair as well as an indication for complete immobilization of sufficient time to permit complete consolidation. In cases of fracture with no displacement he recommends a simple knee cast for one month; in those cases with lateral displacement, compression with clamps under spinal anesthesia, followed by use of a plaster cast for one to one and a half months, and for downward displacement, skeletal traction for four to six weeks.

Cobey [949] recommends a vitallium lag screw of the Lippmann type, with a large oval washer and spur, for accurate reduction and fixation of fractures of the tibial plateau. He describes the screw in detail, the method of open reduction and an application of the lag screw and washer and presents 4 illustrative cases.

Peneiro Sorondo and Ferre [950] discuss the open treatment of fractures of the lateral condyle of the tibia. The illustrations show the stages of the operation for removal of the meniscus between the fragments; the authors operated in 8 such cases in two and a half years. They used two Finochietto pins, long screws and wires for retention in cases of slight displacement, but state that these pins will not prevent lateral spread. They state the belief that a bolt with two nuts is best for retention of lateral spread, and that closed methods of reduction are inadequate because they do not remove the interposed meniscuses and ligaments.

---

948. Vergara, G.: Therapy of Fractures of the Tibial Tuberosity, Arch. Soc. cirujanos hosp. **15**:764-770 (Dec.) 1945.

949. Cobey, M. C.: Lag Screw Fixation in Fractures of Tibial Tuberosity, J. Bone & Joint Surg. **28**:273-276 (April) 1946.

950. Peneiro Sorondo, J., and Ferre, R. L.: Fractures of the External Tibial Tuberosity, Rev. Asoc. méd. argent. **59**:1057-1061 (Sept. 15) 1945.

Fractures of the Shaft of the Tibia and Fibula.—Brumback [951] reviews the records of soldiers with fractures of the tibial shaft in an Army general hospital within the United States. Excluding patients with fractures of the tibial plateau and the malleolar region there were 120 cases, 68 of simple fracture and 52 of compound fracture. The fracture was in the upper third of the shaft in 23, in the middle third in 23 and in the lower third in 74. The results, as listed in the records, were as follows: 75 per cent of patients with simple fractures were returned to duty, 9 per cent were discharged due to disability and 11 per cent were otherwise dealt with (usually transferred nearer home); 46 per cent of patients with compound fractures were returned to duty, 31 per cent were discharged due to disability and 23 per cent were dealt with otherwise. In the entire group, 26 soldiers required operation, 10 on simple fractures (3 of these patients returned to duty) and 16 on compound fractures (10 patients returned to duty). Discharge due to disability did not indicate an unproductive civilian life.

Milgram [952] offers definite procedures for the open reduction of fractures of the tibial condyles and for after-treatment. He states that fractures of the tibial shaft usually have plural lines of fracture which are demonstrable later, during decalcification, and are associated with vascular damage in the bone, which affects the healing. He recommends open reduction of spiral fractures of the tibial shaft, with screw fixation, followed by exercises of quadriceps and toes while in plaster. In discussing cases of fracture of the ankle, he stresses accurate reduction and early operation for those fractures which cannot be reduced by manual attempts. He states that prolonged immobilization and non-weight-bearing for five to six months resulted in revascularization of early aseptic necrosis of the body of the astragalus in 4 cases. He discusses early diagnosis of sprain fractures of the ankle with the use of an injection of procaine hydrochloride into the hematoma and with roentgenograms, taken with inversion of the foot.

[Ed. Note.—This method of diagnosis should not be neglected in the examination of injuries of the ankle.]

Beluffi [953] presents a personal case of isolated traumatic luxation of the fibula. He reviews the literature, noting that luxation of the fibula is rather common in conjunction with fracture of the fibula or tibia or both, but rare in isolation. He found only 22 cases reported since 1900, including his own; in 18 of these the diagnosis was not confirmed

951. Brumback, J. E., Jr.: Mean Disposition of Tibial Shaft Fractures, Am. J. Surg. **71**:532-533 (April) 1946.

952. Milgram, J. E.: Closed Fractures of Leg and Ankle, Bull. U. S. Army M. Dept. **5**:727-731 (June) 1946.

953. Beluffi, E. L.: Isolated Traumatic Luxations of the Fibula, Gior. ital. chir. **2**:157-169 (April) 1946.

roentgenographically. Luxation of the lower end of the fibula was reported once and double luxation (both ends) once, while the remaining 20 cases, including the author's were of luxation of the upper end. The cause of this type of fracture is usually indirect, the condition rarely being directly due to sudden muscular contraction. The diagnosis is easy by roentgenologic examination, and reduction is easy by manipulation. The prognosis is excellent anatomically and functionally.

Malleolar Fractures.—Wilner [954] presents a detailed account, illustrated with drawings and roentgenograms, of the pseudofractures and true fractures that occur commonly in the bones of the ankle and foot. Stress is laid on differentiation between fracture lines and epiphysial lines, on post-traumatic ossification and periarthritic deposits at the distal end of the tibia and fibula and on calcification of veins and arteries.

Hendelberg [955] studied fresh malleolar fractures by fluoroscopy and arthrography on cadavers and live subjects and obtained valuable data on the origin of malleolar fractures, the extent of injury to ligaments and the effects of different manipulations. The results of arthrographic studies correspond well to those of fluoroscopic examination with regard to injuries of the ligaments if done in the first twenty-four hours after fracture. Experiments on cadavers showed that even considerable widening of the anterior part of the tibiofibular mortise does not visualize in roentgenograms and that views in two routine planes do not give a complete picture of the size of the posterior tibial fragment. Thin fragments of the cortical margin, removed with a chisel, were not visualized. Fragments which appeared in roentgenograms as such included varying expanses of articular surface, often very large. The author recommends making it a rule to take a view from the back laterally, to visualize the course of fracture lines in the medial and lateral part of the joint.

O'Donoghue [956] makes a plea for recognition of the fact that open reduction and fixation are necessary in the treatment of fracture of the malleolus when the force has torn the malleolus away from the attachment and carried a strip of fascia into the intervening space, making nonunion certain, or when the spreading of the mortise will result in a permanently weak joint and permanent disability. The author recommends oblique roentgenographic views to reveal separation of the fragments with soft tissue interposition.

---

954. Wilner, D.: Diagnostic Problems in Fractures of Foot and Ankle, Am. J. Roentgenol. **55**:594-616 (May) 1946.

955. Hendelberg, T.: Roentgenographic Examination of Ankle Joint in Malleolar Fractures, Acta radiol. **27**:23-42 (Jan. 31) 1946.

956. O'Donoghue, D. H.: Consideration of Certain Fractures of the Ankle, South. M. J. **39**:367-371 (May) 1946.

Thomasen [957] discusses Niels Hansen's work on fractures of the ankle, with classification according to the position of the foot at the moment of injury, and attempts to clarify certain misunderstandings. Hansen classified fractures in four groups: those which occur with the foot in supination, those with the foot in pronation, those due to external rotation with the foot in supination and those due to external rotation with the foot in pronation. The etiologic diagnosis may be based on the injury to the fibula or to the lateral malleolus, as revealed by roentgenograms. Fractures occurring with the foot in supination show a transverse fracture line in the lateral malleolus; fractures occurring with the foot in pronation show a fracture line directed laterally upward just above the lateral malleolus, sometimes with a small triangular lateral fragment; those due to external rotation with the foot in supination show a long, spiral fracture line running in an upward and backward direction in and above the lateral malleolus, and those due to external rotation with the foot in pronation show a fracture high on the fibula and rupture of the syndesmosis (the interosseous tibiofibular ligament). An unusual and rare type of fracture, presumably produced by exaggerated dorsiflexion of the pronated foot, causes detachment of the medial malleolus and of a large anteromedian fragment on the articular surface of the tibia. Lateral fractures of the anterior and posterior margins of the tibia are caused primarily by tearing of the anterior and posterior ligaments of the lateral malleolus. The technic for reduction, which Hansen worked out on cadavers for each type of fracture, is described, as are the criteria for determining complete reduction. It is important to draw the lateral malleolus forward so that its anterior edge is flush with, or in front of, the anterior margin of the body of the fibula if one is to succeed in closing the anterolateral tibial lesion. The prime rule is to reduce all fractures as though they were of the most severe type. On the basis of etiologic diagnosis, the author states that Hansen's manipulations make possible a reduction of even the most difficult fractures of the ankle. He refers to Hansen's book for results, and, on the basis of these and his own experience, he concludes that Hansen's etiologic diagnosis and reduction technic are of essential importance in the treatment of fractures of the ankle.

Magnusson [958] describes the anatomy of the distal tibiofibular syndesmosis and lists the etiologic classification of malleolar fractures caused by indirect violence (pronation, supination and external rota-

957. Thomasen, E.: Fracture of Ankle; Etiologic Diagnosis and Reposition According to Niels Hansen: Critical Review, Nord. med. (Hospitalstid.) **25**:689-695 (March 29) 1945.

958. Magnusson, R.: Injuries of Distal Tibio-Fibular Syndesmosis in Malleolar Fractures, Nord. med. (Hygiea) **26**:1245-1250 (June 15) 1945.

tion). The author made a critical study of the common roentgenologic methods of diagnosing injuries to the tibofibular syndesmosis. Roentgenologic evidence of injuries to the tibiofibular ligament was present in 412 cases of malleolar fracture in which operation was not performed. Such injury was also present in some cases of fractures of both malleoli due to supination. It should be noted that fractures of the internal malleolus due to pronation were accompanied with injuries to the tibiofibular ligament, which were not evident in roentgenograms until after treatment. The injuries appeared as a change in the lateral contour of the anterior tibial tubercle or in the form of a fragment torn from the anterior tibial tubercle. The author recommends the use of Hansen's etiologic diagnosis as the best way to determine the presence or absence of injury to the syndesmosis. He states that an injury to the syndesmosis is always present in fractures due to external rotation, in fractures due to pronation and in fractures of both malleoli due to supination with medial displacement of the ankle joint. The author stresses the importance of bearing in mind the possibility of injury to the syndesmosis when treating a malleolar fracture, so that diastasis in the malleolar fork may be prevented.

Fractures of the Foot.—Stepanov [959] studied in detail 104 cases of injuries of the lower extremity produced by land mine explosions and classified them into three groups, in which the incidence was as follows: closed injuries of the lower limb and foot, 54 cases (52 per cent); open wounds with multiple injuries to the bones of the foot, 24 cases (23 per cent), and ruptures of the foot and leg, 26 cases (25 per cent). The victim was standing when hit in 92 per cent of cases and crawling in 8 per cent. In 16 cases, the roentgenograms showed injuries of the calcaneus 12 times, of the metatarsal bones 11 times, of the astragalus 9 times, of the tarsal bones 5 times and of the phalanges 2 times. In 22 cases of open injuries, primary amputation was done in 2, infection occurred in 17 (resulting in amputation of the leg in 4, in 1 of which the patient died), improvement was noted under treatment in 6 and amputation was done later in 7. Thus, in 22 cases of open fracture there were 13 amputations. The author states that injuries were caused by the explosion waves and shock rather than by the splinters of the mine. This factor was difficult to recognize without the aid of roentgenograms, which showed the extent of the damage and the fractures.

Albitskiy [960] discusses closed fractures of the foot due to explosion of land mines. He states that there is a typical appearance in these

959. Stepanov, M. M.: Injuries of Lower Extremities Produced by Land Mine Explosion, Khirurgiya, 1945, no. 4, pp. 87-91.

960. Albitskiy, B. A.: Closed Fractures of Bones of Foot Due to Mine Explosions, Khirurgiya, 1945, no. 6, pp. 68-73.

fractures, as follows: shattering or demolition of the calcaneus, with wedging under the astragalus, which may itself be damaged; displacement upward of the rear fragment of the calcaneus by the pull of the achilles tendon and displacement forward of the front fragment by the short muscles of the foot. Luxations and subluxations in Chopart's joint and fracture of the metatarsal bones are explained by the action of the explosive wave on the front part of the foot, the midportion being strengthened by the leg. Fractures of the ankles also occur. The author does not recommend opening of the hematoma, since it leads to infection, but prefers prompt reduction and fixation in plaster casts. The author presents 8 illustrative cases, including instances of fracture of the calcaneus (with and without displacement), the astragalus, the cuboid bone, the metatarsal bones and the lower end of the tibia.

Bershon,[961] in discussing fractures of the feet and toes, points out that failure to follow generally accepted principles of the treatment of fractures may result in healing in malposition and disturbance of the function of nerves, blood vessels and tendons. He describes, in turn, fractures of the os calcis, the astragalus, the scaphoid, the cuneiform bones, the metatarsal bones, the toes and the sesamoid bones, and march fractures. He stresses recognition of accessory bones in the roentgenogram and states that 20 to 25 per cent of the feet of which roentgenograms were made in one series showed accessory bones. He also stresses proper reduction.

Borsotti[962] states that he treated 18 persons with 25 fractures of the calcaneus, who were in a bus under which a land mine exploded. He analyzes the fractures anatomically, discusses the various methods of therapy, reviews briefly the reports in the literature on the treatment and gives a brief case history of each of the 18 patients. He concludes that trauma from below produced characteristic fractures, as follows: Mild trauma produced fracture of the medial tuberosity; more serious trauma produced comminuted fracture of the posterior tuberosity and of the body of the calcaneus, with sinking of the head and subluxation of the astragalus and scaphoid between the anterior part of the calcaneus and the cuboid bone. Immobilization in a plaster cast was used in some cases and traction and casts in others, while amputation was done in the most serious cases.

961. Bershon, A. L.: Fractures of Feet and Toes, Bull. U. S. Army M. Dept. **5**:551-588 (May) 1946.

962. Borsotti, P. C.: The Treatment of Fractures of the Calcaneum Due to Trauma Acting from Below, Minerva med. **1**:272-278 (April 14) 1946.

Cherry [963] reports 16 cases, reported between 1933 and 1940, of fractures of the os calcis in which treatment was by the Boehler method. Two patients could not be traced, 1 had died of tuberculosis four years after the fracture, 1 had multiple injuries and 3 had had type 1 injuries, according to the Watson Jones classification; the author reviews 7 cases of type 2 and 3 injuries (Watson Jones classification) in which the patients were seen four to nine years after the accident. He concludes that the end-result in nearly all cases was the same as before treatment, and that nothing is gained by the rather elaborate Boehler technic. He lists the disadvantages of this method: sepsis introduced through the pin tracts, osteoporosis, possibly due to heavy traction or to trauma by the redresseur, and wasting of the muscles of the calf and thigh.

[ED. NOTE.—The reviewer is inclined to agree with the author's statement that little is gained by accurate reduction in some cases; however, he cannot agree that the method of reduction is responsible for osteoporosis or wasting of muscles.]

Pridie [964] presents a new method for treatment of severe fractures of the os calcis by subperiosteal excision of the entire os calcis. He states that he used this method in 15 cases in three years and that excellent results were obtained in all except those of 2 older men with arteriosclerosis and arthritis. The technic for excision is given, with a description of the method of reinsertion of the achilles tendon in the plantar fascia. In each case, a plaster cast, applied with the foot in plantar flexion, was used for one month, at which time active non-weight-bearing exercises were begun. Weight bearing was begun at six weeks.

[ED. NOTE.—The first example of excision of the os calcis ever seen by this reviewer was that in a middle-aged dentist, who had bilateral excision of the os calcis in early childhood because of osteomyelitis. Function had always been good, and the man wore ordinary shoes without any type of correction. Many men injured in the war lost most or all of the os calcis; results were surprisingly good in cases in which the site was well covered with skin and soft tissue.]

Bado and Cagnoli [965] and Rapaccini [966] report on "duck bill" fractures of the calcaneus. The former authors noted 2 fractures of this

963. Cherry, J. C.: Fractures of Os Calcis, Irish J. M. Sc. pp. 122-125 (April) 1946.

964. Pridie, K. H.: New Method of Treatment for Severe Fractures of Os Calcis: Preliminary Report, Surg., Gynec. & Obst. **82**:671-675 (June) 1946.

965. Bado, J. L., and Cagnoli, H.: "Duck Bill" Fracture of the Calcaneus: Pathogenesis and Therapy, Bol. Soc. cir. d. Uruguay **16**:243-261, 1945.

966. Rapaccini, M.: Contributions to the Study of Fractures of Posterior Superior Angle of the Tuberosity of the Calcaneum with Special Regard to Mechanism of Production, Arch. ortop. **56**:60-76 (July) 1940.

type in 270 cases of fracture of the calcaneus; the latter reports an incidence, for fractures of this type, of 2.64 per cent of all fractures of the calcaneus. Bado and Cagnoli state the belief that only those fractures involving the area of insertion of the achilles tendon can be of the avulsion type, whereas those above this area are caused by a flattening force. In treatment, closed manipulation is satisfactory for those fractures presenting only separation of the posterior ends of the fragments, but unsatisfactory when the fragment has been wedged. The latter type requires open reduction, with severing of the bony wedge by a chisel, after which the fragment is restored to its proper position. Severing of the achilles tendon will not restore a wedged fragment. Rapaccini considers it possible for this type of fracture to occur only in a congenitally predisposed calcaneus, with an unusually high insertion of the achilles tendon.

Negri [967] presents 2 cases of "duckbill' fractures of the calcaneus in patients with tabes dorsalis. In both cases, the fracture occurred as a result of a misstep; the author explains the mechanics of the fracture as the excessive pull on the achilles tendon by sudden and forceful contraction of the sural muscle, in an effort to prevent a fall.

Morrissey [968] reviews the current methods of treatment of fracture of the metatarsal bones and presents 61 cases in which treatment was with a simple molded leather arch, held to the foot by means of adhesive strapping. The method is discussed in detail. All the fractures in this series were due to direct trauma and all patients were men, whose ages ranged from 30 to 61, and who were engaged in various occupations. In 42 cases, there was fracture of only one metatarsal bone, in 11 cases, of 2, and in 8 cases, of 3 or more. Active weight bearing was begun immediately in more than one-half the cases and within a short time in the others. All patients returned to work of some kind within four days, and the majority returned to regular work in less than forty days; by the end of sixty days all had resumed their regular jobs.

[ED. NOTE.—This is a comprehensive report on treatment of fractures of the metatarsal bones; the original article should be consulted by those interested in this subject.]

Fatigue, Strain and March Fractures.—Bernstein and others,[969] who previously reported 307 cases, now add 692 more, among which are

967. Negri, E.: Fractures of Calcaneum, Avulsion Fracture May Be Symptom of Tabes Dorsalis: Two Cases, Anteneo parmense **16**:294-296, 1945.

968. Morrissey, E. J.: Metatarsal Fractures, J. Bone & Joint Surg. **28**:594-602 (July) 1946.

969. Bernstein, A.; Childers, M. A.; Archer, M. C.; Fox, K. W., and Stone, J. R.: March Fractures of Foot: Care and Management of 692 Patients, Am. J. Surg. **71**:355-362 (March) 1946.

724 of march fractures of metatarsal bones. There was no evidence that a relatively shortened first metatarsal played any part in the occurrence of march fractures; the highest incidence occurred during the fifth and sixth week of training at an infantry replacement training center, a time when training was stepped up. Treatment consisted of the insertion of a steel bar longitudinally in the slip sole of the shoe. Only 58 patients did not respond to this treatment; 13 of these were hospitalized, and 45 were excused from training until the fracture healed. All 58 eventually finished training and were sent overseas. The author observed 426 fractures in the right foot and 298 in the left. The roentgenologic diagnosis is fully discussed.

Leveton [970] reports 12 march fractures of the pelvis and the lower long bones, excluding the metatarsals. Six were fractures of the tibia, 1 of the fibula, 2 of the femur (1 of the shaft and 1 of the neck) and 3 of the pelvis. The etiologic factors were obscure, but the author states the belief that the fractures were due to muscular fatigue or muscular imbalance. The ideal treatment was bed rest and the prohibition of early weight bearing. Delayed union was not encountered. The roentgenographic appearance was that of an "ice crack" fracture or of callus formation.

Levitin [971] reports 64 cases of march fracture of the articular surface of the tibial plateau. All the fractures were associated with pain. Forty-six cases were of fracture of the internal condyle and 18 were of the external condyle, a ratio of 2.6 to 1. The right knee was involved slightly oftener than the left. This fracture differs from other march fractures in that no bony callus forms to obliterate the fracture line during an observation period of six months. These injuries occur in civilian life but are so trivial that they are not usually examined roentgenologically until after osteoarthritic changes have taken place.

McPhee and Franklin [972] present 6 cases of march fracture of the fibula and 1 of the foot in athletes at Princeton University.

Nordentoft [973] presents 4 cases of march fracture, 1 each in the pubic ramus, the spinous process of the last cervical vertebra (clay shoveler's disease), the metatarsal bone and the femur.

Childress [974] presents a case of march fracture of the second metatarsal in a boy of 7. To this interesting case report the author appends

970. Leveton, A. L.: March (Fatigue) Fractures of Long Bones of Lower Extremity and Pelvis, Am. J. Surg. **71**:222-232 (Feb.) 1946.

971. Levitin, J.: March Fractures of Articular Surface of Tibia and Its Relation to Osteoarthropathy, Radiology **46**:273-275 (March) 1946.

972. McPhee, H. R., and Franklin, C. M.: "March Fracture" of Fibula in Athletes, J. A. M. A. **131**:574-576 (June 15) 1946.

973. Nordentoft, J. M.: March Fracture; Fatigue Fracture; Pseudofracture: Four Cases, Ugesk. f. læger **107**:391-394 (May 24) 1945.

974. Childress, H. M.: March Foot in a Seven Year Old Child, J. Bone & Joint Surg. **28**:877 (Oct.) 1946.

the following warning: "Had this patient been examined during the acute stage, a diagnosis might have been made of osteomyelitis or even of osteogenic sarcoma. March fracture always should be considered in osteoblastic lesions of the metatarsal bones, even in young children."

INJURY TO NERVES

Spurling [975] comments on the failure to treat injuries to nerves in patients with combined lesions of the nerve and bone during the North African and early European campaigns in the last war, with resultant useless members that could not be repaired in at least 20 per cent of cases. A program to provide early nerve suture was begun in December 1944; it entailed removal of patients to a neurosurgical hospital, early delayed closure of the primary wound and elective operation three weeks after healing of soft tissues. At the time of nerve suture, bone repair was done by the orthopedic member of the surgical team. About 10 per cent of patients required shortening or internal fixation of bones; 60 per cent required end to end suture of the damaged nerves and the remainder were treated by simple external and internal neurolysis. Twelve per cent of a total of 300 patients showed spontaneous recovery of the nerves during the waiting period. Final results are not given because of too short a follow up; prospects were excellent for recovery of the radial and sciatic nerves but less satisfactory for the recovery of the brachial plexus and the median and ulnar nerves.

COMPOUND FRACTURES

Brav and Fetts [976] studied 82 cases of gunshot fractures of the femoral shaft in a hospital in North Burma. Eighty-five per cent of patients were Chinese. There was a 4.9 per cent mortality; bone union occurred in 96 per cent of the cases.; good functional results were obtained in 67 per cent of the followed cases, fair results in 24 per cent and poor results in 9 per cent. Skeletal traction in balanced suspension is the method approved by the authors for fixed installations; the use of a plaster spica is their choice for temporary immobilization. Traction should be continued until there is roentgenologic evidence of bony union; the average time required was twelve weeks. Motion of the knee joint should be encouraged after eight weeks.

Obletz [977] recommends "90-90-90 traction" as an aid to operative management, as it permits easy approach to all soft tissue wounds

975. Spurling, R. G.: Early Treatment of Combined Bone and Nerve Lesions, Physiotherapy Rev. **25**:287-288 (Nov.-Dec.) 1945.

976. Brav, E. A., and Fetts, W. T., Jr.: Gunshot Fractures of Femoral Shaft, Surg., Gynec. & Obst. **82**:91-100 (Jan.) 1946.

977. Obletz, B. E.: Vertical Traction in Early Management of Certain Compound Fractures of Femur, J. Bone & Joint Surg. **28**:113-116 (Jan.) 1946.

as well as to the fracture focus in the treatment of compound fractures of the femur. The hip, knee and ankle are all in 90 degree flexion; the patient is in dorsal recumbency, with Kirschner wires inserted through the condyles of the femur or the tibial tubercle, for vertical traction to an overhead bar; for operative procedures, the foot is held by a sock attached to the overhead bar. The same position can be maintained in bed with a 10 pound (4.5 Kg.) weight horizontally on a standard Pearson knee attachment, with foot rest. The author recommends the use of this position for only three to four weeks, after which conventional splints should be used.

Soto-Hall and Horwitz [978] review 163 cases of fractures of the femur, in which 117 were compound and 46 simple fractures; 41 were treated by internal fixation and 122 by suspension traction. The authors conclude that early and adequate débridement is the most vital factor for successful treatment in compound fracture, that chemotherapy may control infection but is useless in the presence of necrotic tissue and that delayed wound suture and conservatism in the removal of large bone fragments are desirable. Extremely gratifying results were obtained with traction in balanced suspension. Early internal fixation in the presence of an open wound was hazardous. Early use of active exercise with carefully supervised resistive exercises aided knee function.

OPERATIVE FIXATION OF FRACTURES

Medullary Nailing.—Much interest has been shown in this treatment in the past few years. D'Aubigne and Lance [979] used intramedullary nailing in 17 cases of diaphysial fracture of the femur. Treatment in all cases was by opening of the focus of the fracture. The authors state that they prefer to insert the nail from the fracture into the proximal fragment, reducing the fracture and then running the nail into the distal fragment. They recommend a nail used by Ivar Palmer of Stockholm. They state that they operated thus in 17 cases of ancient fractures of the femur (5 fractures had previously been plated). Fractures in 3 cases were recent and loss of bone had taken place in 2. Of the patients in the remaining 12 cases, 8 of which had war wounds, 11 had normal consolidation in three months; 3 of these had slightly hypertrophic callus. Knee motion was almost complete in 5, and greatly limited in 7.

Boppe and Adam [980] report the use of Küntscher's intramedullary nailing in the treatment of 20 fractures of the femoral diaphysis, 14 of

978. Soto-Hall, R., and Horwitz, T.: Treatment of Compound Fractures of Femur, J. A. M. A. **130**:128-134 (Jan. 19) 1946.

979. d'Aubigne, R. M., and Lance, P.: Results of Medullary Nailing in Fractures of Femur, Mém. Acad. de chir. **72**:370-372 (June 19-26) 1946.

980. Boppe, and Adam: Küntscher Nailing in Fractures of Femur, Mém. Acad. de chir. **72**:372-374 (June 19-26) 1946.

which were recent and 5 ancient. Pseudarthrosis of the femur occurred in 1 case six and a half months after nailing. Of the 14 cases of recent fracture, 7 were in adults and 7 in children. In 7 cases the nailing was percutaneous, and in 7 the fracture site was opened. The authors were striving to improve their technic so that percutaneous nailing could be used in all cases. The cases were followed for two to eighteen months after operation. In most cases the nails were still in situ, and healing in all was without incident.

Huet [981] makes it clear that he does not favor the use of the Küntscher nail. Basing his argument on the experiences of his pupils who were forcibly detained in German hospitals for some time and who saw the Küntscher method used, he counters all claims for intramedullary nailing. He concludes that the Küntscher method is not an improvement over osteosynthesis with plate and screws or over the older methods.

Leveuf and Laurence [982] report 13 cases of intramedullary nailing of diaphysial fractures of the femur in children from 2 to 13. In all cases, it was necessary to open the fracture site. The authors used the angle nail made by Drapier and the Rocher round nail; nails were removed in all cases in three to four months. Late results were excellent. The authors state the opinion that indications for intramedullary nailing are irreducible fractures of the middle or upper third of the femur, and vicious malunion and pseudarthrosis.

Uffreduzzi [983] reports his experiences and states that Küntscher's method has the decided advantage of interfering less with consolidation and with callus formation than any type of appliance used on the outside of the bone. The author prefers a long, slender rod, which he believes causes very little damage to the contents of the medullary canal. It is possible to insert the prosthesis at a distance from the focus of the fracture. Favorable results are reported, and the author states that this method can be applied to gunshot wounds that are not too badly contaminated or infected.

Jeanneney, Magendie and Tingaud [984] report a very interesting series of cases of fracture in which treatment was by the Küntscher method

981. Huet, P.: Küntscher Nailing in Fractures of Diaphysis of Femur, Mém. Acad. de chir. **72**:400-403 (July 3-10) 1946.

982. Leveuf, J., and Laurence, G.: Results in Intermedullar Nailing by the Method of Küntscher in Fractures of the Femoral Diaphysis, Mém. Acad. de chir. **72**:368-369 (June 19-26) 1946.

983. Uffreduzzi, O.: Fixation by Intramedullary Nailing, Gior. d. r. Accad. di med. di Torino (parte seconda) **105**:89-95 (July-Sept.) 1942.

984. Jeanneney; Magendie, and Tingaud: Late Results of Medullary Nailing of Diaphyseal Fractures According to Küntscher Method, Bordeaux chir. **3-4**:63-74 (July-Oct.) 1943.

and that of Rocher, using a solid steel rod. The authors state that there was excellent tolerance of the rod in 3 cases. Signs of decalcification in 1 case were probably due to the mobility of the rod, and in 2 cases in which ordinary steel was used there was oxidation. The authors state the opinion that intramedullary nailing, whether done because of destruction of the medulla or for some other reason, appears to cause a retardation in the callus formation. For this reason the fixation should be continued at least a month longer than the usual period. The authors recommend the method as ideal in treatment of fractures of the bones of the forearm and of the femoral shaft.

Rocher [985] reports on 22 cases, all of difficult fractures or of failures in treatment by other methods. He states that no patient of his has ever had a painful sequela following nailing or withdrawal of the nail; neither infection nor fat emboli have been observed. He reports 2 cases in which there was a loss of bone substance; osseous tissue grew out along the nail and filled the loss completely. He is of the opinion that, with sufficient experience, this method is the simplest and best for treating the average fracture.

In view of the controversy over the intramedullary pegging of bone, Chigot [986] conducted a series of experiments on rabbits and dogs, using autoplastic, homoplastic and heteroplastic pegs. In certain animals he observed fusiform periosteous hypertrophy, noted by others in human patients; the growth was fleeting and inconstant. Resorption of the peg was remarkably clear in certain instances, but irregular. Histologic study showed a fibrous reaction of the medulla, but complete restoration and no cicatrix. The periosteum, not the medulla, is the bone-making organ, and an intramedullary foreign body is much less harmful to the bone than a periosteal plate. The author discusses changes in the materials used for intramedullary pegs since his previous report in 1937; he now states a preference for bone and uses dealbuminated pegs. He states that he finds the use of the Küntscher nail difficult on the femur. In the treatment of fractures of both bones of the forearm, he states that he prefers to use a Kirschner wire in the ulna and a dealbuminated bone peg in the radius. The wire is inserted first; it is pliable enough to permit angulation of the radius for insertion of the bone peg. The extremity is treated in a plaster cast.

[Ed. Note (W. G. S.).—Here we are back to the intramedullary bone graft.]

---

985. Rocher, C.: Medullary Nailing of Long Bones: Reflection on Twenty-Two Cases, Bordeaux chir. **1-2**:80-81 (Jan.-April) 1944.

986. Chigot, P. L.: Intramedullary Diaphysial Osteosynthesis by Means of Pegging, Presse méd. **54**:89-91 (Feb.) 1946.

Soeur,[987] in an excellent article, discusses the historical background of the intramedullary fixation and calls attention to the fact that Lambotte has been using the method since 1907 without recognition of the fact by American surgeons. The author cites the objections for and against the method and takes up individually the treatment of fractures of the various long bones, discussing the method to be utilized in managing each of these fractures. He recommends intramedullary fixation because it fulfills the three principles of treatment, namely, reduction, which is usually excellent; fixation, which is strong and firm, and mobilization, which is rapid. In 55 cases of fracture reported, there were 23 of the shaft of the femur, 10 of the leg, 9 of the humerus and 13 of the forearm; the results were excellent. The author feels that the method is particularly applicable to fractures of the femur and forearm and that it solves problems not met satisfactorily by other methods. He does not, however, advise its use in the treatment of compound fractures.

Floding [988] reports on 15 cases in which treatment was by intramedullary nailing according to the method of Küntscher. The study consists of a review of Küntscher's method, its advantages and the indications for its use as given by Küntscher himself, together with a description of the instruments necessary and a number of case reports. In this discussion, there is comparatively little in the way of critical evaluation of the procedure.

Magnant [989] reports on treatment of 13 fractures by the Küntscher method and states that it is better to use a Kirschner wire than a heavier pin in the treatment of fractures of the clavicle. The author states that he prefers the cylindric rods of Rocher. Fractures of the femur may be nailed without opening the fracture. Of 6 cases in which the leg was involved, a small opening at the site of fracture was necessary in only 3. Magnant stresses the noninterference with callus formation, the much earlier restoration of function in the extremity and the excellent tolerance of the nail in the tissue in his cases in which treatment was by this method.

Leger and Crepin,[990] on the other hand, report 11 cases in which they used the Küntscher nail. In only 1 case in this series was the fracture nailed without opening the site of the fracture. The authors

987. Soeur, R.: Intramedullary Pinning of Diaphysial Fractures, J. Bone & Joint Surg. **28**:309-331 (April) 1946.

988. Floding, A.: Fractures of Long Bones Treated wtih Medullary Nailing According to Küntscher, Nord. med. **30**:1179-1183 (May 31) 1946.

989. Magnant: Küntscher Method of Nailing Long Bones: Late Results, Mém. Acad. de chir. **72**:378-379 (June 19-26) 1946.

990. Leger, L., and Crepin, G.: Küntscher Nailing, Mém. Acad. de chir. **72**:375-376 (June 19-26) 1946.

defend this procedure on the ground that more damage would have been done in the treatment of fractures of great displacement by manipulation and closed reduction; in 1 case the radial nerve was caught between the fragments. They state the belief that the best indication for this method is pseudarthrosis and that spiroid fractures of the leg are a contraindication. The nailing of a fracture of the humerus is the easiest use of Küntscher's method. The nailing of the femur is facilitated by the use of the scissors position recommended by Christian Rocher.

Guides and Devices for Internal Fixation.—Stone [991] presents a guide for the nailing of fractures of the femoral neck, consisting of a steel bar attached to and extending upward from a nail driver at 90 degrees and a clamp which holds the guide rod parallel to the nail driver. The author claims that its advantages are that the direction of the nail is visible to the operator, that no part of the guide enters the operative wound, that operative time can be shortened and that the use of the guide eliminates repeated roentgenographic check-ups.

Hopkins [992] presents a detailed description of a block guide which is attached to the external surface of the femur after reduction to serve in directing the proper placement of a nail in the femoral head and neck.

Fractures Treated by Continuous Wire Traction.—Kirby and Fitts [993] report their experiences in 342 cases in which treatment was given at a general hospital in India. In this series, 194 patients were treated with Kirschner wires, 95 with Steinmann pins and 52 with Roger Anderson pins with fixed or balanced traction. Among those patients treated with Kirschner wires, 4 wires grew loose from the bone and 1 broke in fourteen weeks. The bow slipped and the wire pulled out in eight weeks in an additional case. With the Steinmann pin the results apparently were quite satisfactory, although an abscess developed in 1 case and there was transient peroneal paralysis in 2 cases. In the group treated with the Roger Anderson pin 3 pins became loose. In none of the cases did the complications have any significant effect on the course of the treatment or the final result. The authors consider that the use of transfixion pins and wires for skeletal traction is a safe and reliable procedure.

---

991. Stone, M. M.: Visible Guide for Nailing Intracapsular Femoral Neck Fractures, Am. J. Surg. **71**:100-102 (Jan.) 1946.

992. Hopkins, H. H.: Intertrochanteric Fractures and Fractures of Neck of Femur: A Guide and Method of Procedure for Accurate Placement of Nail, J. Bone & Joint Surg. **28**:244-249 (April) 1946.

993. Kirby, C. K., and Fitts, W. T., Jr.: Incidence of Complications in Use of Transfixion Pins and Wires for Skeletal Traction, Ann. Surg. **123**:27-31 (Jan.) 1946.

Schildt,[994] in a comprehensive article covering his experience in the treatment of 540 fractures by wire traction, states that complications in the form of nerve injuries, cutting of the wires, infection or necrosis were encountered in only 10 per cent of the cases. Prognosis of the nerve injuries is likely to be very favorable. Cutting of the wires through tissue was noted in 18 cases; the disadvantage of this is slight unless the cutting is in the lower end of the femur, when it may lead to menacing and serious complications because of damage to the knee joint. Infections without cutting of the wire were observed in 30 cases of 504 (6 per cent), but the infection was slight to moderate and had no disastrous effect on the course of the treatment. The author states that wire traction in the calcaneus is practically free of risk. Complications in cases in which wire traction is used in the tuberosity of the tibia are fairly numerous, but not serious. The author calls attention to the necessity of preventing lateral slipping in the wire and states that the points of exit and entrance must be protected with a snug bandage to assist in the prevention of infection.

Dwyer and Murry[995] review the treatment of fractures at the Northern Permanente Hospital Vancouver, Wash., from September 1942 to December 1944. In this period, 1,418 fractures were seen. Of this number, 131, or 9.2 per cent, were treated by skeletal traction and 121, or 8.5 per cent, by dual pin fixation. The Roger Anderson equipment was found most desirable for use with the dual pin method. Kirschner wire and the Kirschner-type tautner were used for skeletal traction. Continuous skeletal traction was used mainly for fractures of the hands and feet. Dual pin fixation was used chiefly in fractures of the tibia, fibula, femur, mandible, os calcis and humerus. In this series, osteomyelitis developed in 2 cases of hematogenous origin and 1 of external origin. There were 4 instances of delayed union, 4 of malunion and 3 of nonunion in the entire series, or unsatisfactory results in 4.4 per cent of the cases.

Scott[996] also makes a plea for greater use of the external fixation treatment of fractures, stating that it is much easier and less hazardous than some of the older and more generally accepted methods of treatment. The author states that the treatment of compound fractures is facilitated by this method. He cites as an advantage the reduction in the number of stiff joints after immobilization.

---

994. Schildt, E.: Complication of Wire Traction Treatment, Nord. med. (Hygiea) **29**:301-307 (Feb. 8) 1946.

995. Dwyer, F. J., and Murry, D. H.: Therapy by Skeletal Traction or Dual Pin Fixation: Two Hundred and Fifty-Two Cases, Northwest Med. **45**:173-177 (March) 1946.

996. Scott, I. H.: External Skeletal Fixation, Am. J. Surg. **72**:723-733 (Nov.) 1946.

Roberts[997] reports the treatment of mandibular fractures by means of the Roger Anderson external splint. The author says that use of this apparatus provides an excellent form of treatment for certain types of jaw injuries. He states the belief that the method should be used only by responsible surgeons working under proper conditions, lest it be discredited; it is not the method of choice when simpler methods will give equally satisfactory results. The author's opinion is shared by Burke, Murphy and McNichols,[998] who state that Roger Anderson apparatus is particularly adaptable to the treatment of certain types of mandibular fractures which cannot be treated satisfactorily by other methods.

GENERAL FACTORS IN TREATMENT OF FRACTURES

Dickson,[999] in a practical article, calls attention to the use of physical therapy in the treatment of fractures. The place of occupational therapy is stressed.

Engh[1000] reports on a series of roentgenograms of fractures in and about the joints, in the treatment of which he used vitallium screws for fixation. The author does not recommend this method as one of choice but states that it is possible to fix fractures in these areas by this means and that the end results can be excellent.

Anopol[1001] stresses that treatment of fractures should be simple, direct and practical and emphasizes the value of fundamental principles of therapy as applied to each individual case. He reminds the reader that good reduction is not enough when the soft tissues are injured, that methods used experimentally on animals cannot be transferred directly to the treatment of human beings and that the functional position of each joint must be considered when there is a possibility of ankylosis. He deplores the present trend of the "gadget treatment" of fractures.

Verbrugge,[1002] in a comprehensive article concerning factors influencing callus formation in open fixation of fractures, emphasizes the

997. Roberts, W. R.: Control of Mandibular Fragments by External Fixation, Brit. Dent. J. **80**:257-269 (April 18); 291 (May 3) 1946.

998. Burke, H. D.; Murphy, D. L., and McNichols, W. A.: Skeletal Fixation of Mandibular Fractures: Five Cases with Nine Fractures, Arch. Surg. **51**:279-282 (Nov.-Dec.) 1945.

999. Dickson, F. D.: Physical Therapy in the Treatment of Fractures, Rev. radiol. y fisioterap. **13**:17-21 and 35 (Jan.-Feb.) 1946.

1000. Engh, O. A.: Screw Fixation of Fractures, J. Internat. Coll. Surgeons **9**:144-151 (Jan.-Feb.) 1946.

1001. Anopol, G.: Therapy in Fractures, Bull. internat. serv. san. **19**:91-93 (March) 1946.

1002. Verbrugge, J.: Factors Influencing Callus Formation in Open Fixation, J. Bone & Joint Surg. **28**:535-543 (July) 1946.

importance of performing open fixation as soon as possible after injury. When operation is not carried out until fifteen days after the fracture the optimum time is lost for early callus formation and for early union of the fracture. The author also discusses the nature of the internal fixation used and its physiologic application to the fracture. He states that other factors influencing callus formation are early function, sympathectomy, ganglionectomy, massage, the administration of calcium and short wave diathermy.

Darrach,[1003] in a well written, didactic article, emphasizes nothing new but calls attention to the old principles which underlie all treatment of fractures, namely, (1) reduction of secondary trauma to a minimum, (2) sufficient restoration of normal form to meet the requirements of the specific patient, (3) rest for the fractured part during the healing process, (4) maintenance and restoration of the function of the soft parts and (5) maintenance of the morale of the patient. The author also emphasizes the fact that the patient must be treated as an individual human being and not simply as a fractured bone of one kind or another.

Sweetapple [1004] discusses the clinical features, etiology and treatment of Sudeck's atrophy but fails to add any definite information not already known. [ED. NOTE (W. G. S.).—This is a general article and reviews the subject well.]

Hojensgaard [1005] calls attention to the frequency of secondary dislocations in cases of fractures of the distal end of the radius. In a series of 217 cases of such fractures, redislocation was noted in 52 cases, or 24 per cent of the total. The author suggests that the average rate of incidence may be still higher. These fractures are classified in seven groups, according to type. Dislocation occurs most frequently in cases in which a distal fragment shows volar dislocation and in comminuted Colles' fracture. A statistical tabulation shows that redislocation is most likely to occur in women past 60. The author recomends the following procedure as a means of preventing redislocation: (1) roentgenographic control; (2) avoidance of a loose bandage, due to swelling at the time of application (replacement with a snug bandage should be done as soon as possible); (3) application of a well padded circular cast and (4) fixation for an adequate period (four to five weeks as a minimum.)

1003. Darrach, W.: Presidential Address, Ann. Surg. **124**:607-616 (Oct.) 1946.

1004. Sweetapple, H. A.: Sudeck Atrophy, M. J. Australia **2**:581-584 (Oct. 26) 1946.

1005. Hojensgaard, I. S.: Frequency of Secondary Dislocation in Fractures, Nord. med. (Hospitalstid.) **28**:2135-2139 (Oct. 19) 1945.

Teece,[1006] in discussing the procedures and attitudes in handling orthopedic disorders in industrial patients, gives no specific formula to solve this problem. He states that the attitude of the medicolegal patient differs according to race and occupation. Aside from this factor, there are two types of patients who are not often encountered in ordinary practice, namely, the fulsome, cooperative patient and the suspicious, exaggerating patient. The former talks volubly of his injury, and the latter practically refuses to discuss it, apparently believing that the examining physician is in league with the insurance company and striving to deprive him of his rights and his compensation. As for actual treatment of the orthopedic conditions seen in industrial practice, there are no notable differences as compared with treatment in the rest of the community. The author states the belief, however, that the chief emphasis is on function rather than on appearance. Injuries to fingers are very common in industrial work, and the question of early amputation frequently arises. The object of primary treatment should always be to save as much as possible of every digit. The author believes that malingering is rather rare but that some patients, in the course of long treatment, become afraid to use the injured part and assume that recovery may not be complete. Other patients acquire the habit of idleness during a long period of inactivity with compensation and lose the will and desire to return to work.

COMPOUND FRACTURES

Rounds [1007] discusses treatment in 551 cases of war injuries recorded in a general hospital in England, in which various modifications of the Orr-Trueta treatment were carried out. He states that successful secondary closures can be performed after the Orr treatment has been meticulously carried out at the front station. He suggests that the best time for secondary closure is on the fourth or fifth day after injury; the average time of closure in this series was on the twelfth day. Healing took place in 90 per cent of the cases; it was apparently unaffected by the use of penicillin, although the drug was used in the worst cases.

Eaton [1008] reports on the routine treatment of compound fractures of the long bones in the campaigns of World War II. He stresses the importance of first aid and shock therapy even before the patient is moved to the clearing company from the battalion aid station. The first operation performed at the forward station was careful débridement

1006. Teece, L. G.: Special Characteristics and Requirements of Orthopædic Surgery, M. J. Australia **2**:580-581 (Oct. 26) 1946.

1007. Rounds, R. C.: Delayed Suture of Wounds Associated with Fractures, Rocky Mountain M. J. **43**:216-219 (March) 1946.

1008. Eaton, G. O.: Overseas Treatment of Compound Fractures of Long Bones, J. Bone & Joint Surg. **28**:434-439 (July) 1946.

of the wound, consisting of thorough exposure and exploration of all tracts and excision of all devitalized tissues, decompression and aeration of the wound, generous incision and relaxation of the fascial layers (with great care to preserve as much skin as possible), counterincisions for dependent drainage and complete removal of all fragments of bone completely denuded and unattached. The author recommends not suturing the injured tendon or nerves but marking them for later suturing. After débridement the wound is left wide open, with no attempt at partial closure. Eaton stresses particularly that the wound must not be closed in the early stage at the forward station.

Bintcliffe,[1009] who was stationed at a base hospital rather than at a forward station, describes the receipt of patients. He emphasizes the importance of using penicillin. He is particularly concerned with the subject of delayed primary suture or so-called secondary suture of the wounds which have undergone careful and prompt débridement and been left open. Further limited débridement was carried out if necessary but often was totally unnecessary. The author describes 30 cases in which suturing was done one to eighteen days after injury. In 17 cases the wound was completely healed in fourteen days; in 9 cases there was some delay in healing, and in only 4 cases was there failure of the wound to heal, accompanied with breaking down, necrosis or sequestrum formation. Bintcliffe, too, stresses the importance of the surgical operation performed at the front station, after which the wound is left open, no attempt being made to close it.

Hampton[1010] discusses 332 cases of fractures in which treatment was by various types of delayed internal fixation, which are described. He suggests that all these forms of internal fixation should be carried out only after primary or secondary closure and healing of the wound. The author provides a detailed discussion of 20 cases, with illustrations.

Novachenko,[1011] in discussing fractures treated at the finish of the war, states the belief that it is possible to note certain peculiarities or characteristics of gunshot injuries as opposed to those caused by other etiologic agents. He describes the classic form of this type of the fracture as a butterfly wing; the fracture is shattered in character, leaving sequestrums of bone, which may be a complicating factor. This type is characterized also by pronounced displacement of the fracture and by the scattering of fragments of bone throughout the soft tissue. Another peculiarity is that of bone regeneration. The author notes that

1009. Bintcliffe, E. W.: Delayed Closure of Compound Fracture Wounds, Post-Grad. M. J. **21**:338-348 (Dec.) 1945.

1010. Hampton, O. P.: Delayed Internal Fixation of Compound Battle Fractures in the Mediterranean, Ann. Surg. **123**:1 (Jan.) 1946.

1011. Novachenko, N. P.: Characteristics of Gunshot Fractures, Vrach. delo **24**:47-52 (Dec. 1) 1944.

gunshot fractures apparently healed as fast as closed fractures, in spite of the general belief to the contrary. There was, however, certain characteristic lingering of different stages of callus formation, the completion of which seemed to take somewhat longer than usual. The author recommends treatment as early as possible, directed primarily toward prevention of infection and secondarily toward repair of the fracture; this type of fracture can be treated by reduction, use of a plaster cast, skeletal traction or various other methods.

Faltin [1012] directs his attention particularly to two types of fractures. The first group is composed of those about the face; the author stresses the importance of proper first aid and early treatment at a field hospital, preliminary to definitive treatment at a special hospital for maxillary surgery. The sooner the treatment is begun, the better result will be obtained. The second group, in which the author has particular interest, is that composed of fractures of the hands and fingers. The author stresses the importance of special centers where definite treatment can be given to the hand by those especially skilled, since passive treatment has too often resulted in useless fingers.

Carney, Fitts and Kirby [1013] direct their attention to gunshot injuries of the joints as opposed to fractures of the long bones, noting that treatment of these injuries is usually difficult and that results are often disappointing. The authors studied 134 cases of gunshot wounds of the major joints in which there was a complicating fracture of the adjacent bone. No particulars are given because the follow-up was too short to be of any value in analyzing the permanent result. These authors, too, stress the importance of careful débridement and removal of all foreign bodies. Ordinarily the capsule should not be closed primarily but by secondary closure, in order to minimize infection. The authors state that fusion of the joint should be postponed, since improvement will often follow after many months, or even years.

Compere [1014] discusses the treatment of compound fractures in civil life with particular emphasis on the way they have been maltreated in many instances. He gives a detailed outline of the care of the compound wound, stressing the importance of the care given by the general practitioner who sees these wounds immediately after their occurrence; he recommends careful splinting before arrival at the hospital, careful débridement and lavage. He discusses the problem of primary or secondary closure of the wound, giving the indications and contraindications for each procedure.

1012. Faltin, R.: Contribution to the Solution of Several Problems in Military Surgery, Nord. med. **17**:91-98 (Jan. 16) 1943.

1013. Carney, P. W.; Fitts, W. T., and Kirby, C. K.: Gunshot Wounds of the Major Joints, J. Bone & Joint Surg. **28**:607-615 (July) 1946.

1014. Compere, E. L.: Adequate Treatment of Compound Fractures, Illinois M. J. **88**:289-293 (Dec.) 1945.

[Ed. Note (W. G. S.).—In considering all these articles together, certain major points of agreement are at once evident. The authors are unanimous in stating, at least with regard to war surgery, that grossly contaminated gunshot injuries should be treated by débridement of the wound, after which the wound should be left open and careful support supplied to the wound and the extremity; secondary or delayed closure should be done from one to two weeks subsequent to the original operation. Disagreement exists as to whether or not loose fragments of bone should be removed, the majority of writers stating the opinion that they should be. There is considerable unanimity in the opinion that tendons and nerves should be marked at the primary operation, but should not be sutured, and that internal fixation was inadvisable at the time of the secondary closure but should be done after healing. All the authors stressed repeatedly the importance of general systemic care of the patient.]

In concluding this subject, it is well to mention an article by Cleveland,[1015] in which he gives a comprehensive review of the treatment of the wounded, in general, in World War I and in World War II. The author describes the preparation at the orthopedic centers for care of the wounded with injuries of bones and joints, the fixed hospitals in the zone of communication, the treatment of severe multiple fractures and the healing of compound fractures, amputations and neurosurgical injuries and injuries to the hands. He makes the following observation:

> Having served as a medical officer in both wars, it may be permissible to make a few comparisons. The 25 years which elapsed between the wars has seen progress in the training of the young surgeons and this was reflected in the fact that more and better trained surgeons were available to do better surgery. There never were enough to completely fill all the existing vacancies, but the situation was vastly improved over World War I. In the European Theater the general level of care of bone and joint casualties was vastly improved. Superior care was unquestionably rendered by many of the affiliated hospitals of World War I, but in other less favored units it left much to be desired. There was a more complete and general understanding of resuscitation in World War II. No blood or plasma was available or used in most of the Army hospitals in World War I. The great stocks of plasma and whole blood which were made available and were used so extensively saved many of the wounded who would otherwise have succumbed.
>
> The evacuation of the wounded in World War II was more rapidly accomplished.
>
> The overseas hospitals were very much better equipped for their work in this war. The low incidence of infection was probably due to better surgery in the forward areas. In this matter of lower infection, the role of sulfonamides and penicillin is not absolutely clear. These new drugs probably exerted a beneficial effect, but controlled experimental data is not available.

1015. Cleveland, M.: Orthopedic Surgery in the European Theater of Operations, Ann. Surg. **124**:188-200 (Aug.) 1946.

The European Theater was singularly fortunate in having a Chief Surgeon whose sole aim was to improve the standard of care of the sick and wounded American soldier. Nothing deterred him from this aim. The professional service division had a group of consultants who worked harmoniously as a team under inspiring leadership of the Chief Surgeon and the Chief Consultants in Surgery and Medicine.

FAT EMBOLISM

Warren [1016] presents a review of 100 consecutive fatal cases of fat embolism recorded in the files of the Army Institute of Pathology in four years (1941 to 1944); 82 per cent of these were due to fractures of the tibia or the femur. The author calls attention to the fact that embolism is due not to aggregation of circulating fat, but to quantities of fat set free from bodily deposits. Death was instantaneous in 9 of the cases; it occurred after symptoms of immediate origin in 17 cases and was delayed in 58. The occurrence of fat embolism is apparently uninfluenced by the nutritional state of the patient. The condition may be recognized by development of pulmonary or cerebral symptoms following fracture or extensive injuries of soft parts, or manipulation of a fracture. The renal fat embolism may be pronounced, but renal failure is not the cause of death. Many nonfatal cases of fat embolism are not recognized, and many fatal cases may be unrecognized unless a search is made for the cause of death.

Lindsay and Moon [1017] present 3 cases in which bone marrow embolisms were found in the arteries in the lungs of men who died after accidents in which they received multiple fractures. The embolisms were found in examinations of sections taken from the lungs at necropsy. The authors point out that although some 600 cases of fat embolism have been reported, the condition usually occurring after fracture of the long bones, only 1 case of associated bone marrow embolism to the lungs has been reported. This report is of interest, but no particular recommendation for prevention or treatment is included.

FRACTURES OF THE SPINE

Daniels [1018] discusses, in some detail, the management of fractures and dislocations of the spine in warfare, basing his article largely on his personal experience while in the Navy. He discusses many problems rather unique to the service, including evacuation of the injured person and his rapid transportation to a first aid station. In most instances patients were examined at first aid stations within fifteen minutes after injury. The author seems well satisfied with the method of handling

1016. Warren, S.: Fat Embolism, Am. J. Path. **22**:69-87 (Jan.) 1946.

1017. Lindsay, S., and Moon, H. D.: Bone Marrow Embolism Following Fracture, J. Bone & Joint Surg. **28**:377-380 (April) 1946.

1018. Daniels, J. T.: Fractures and Dislocations of the Spine in Warfare, Am. J. Surg. **72**:414-423 (Sept.) 1946.

this type of injury in the service and points out that it was greatly improved over that in World War I. A rather detailed description is given of the method of handling these patients, both on land and on sea, and of the causative factors in various types of war injuries. Laminectomy is recommended when there is evidence of any progression of cord dysfunction with pressure of a fragment, either of bone or of a foreign body, on the cord, or when there is an irreducible dislocation, particularly if it involves the area of the lower cervical and upper dorsal portions of the spine.

Guthkelch [1019] calls attention to the fact that the ordinary fracture and dislocation of the cervical portion of the spine must be reduced by both traction and extension. He describes a method of successful reduction by skeletal traction. Some points of technic are different from those ordinarily suggested: The traction apparatus is placed in the skull, forward of the external auditory canal, thus increasing the extension on the upper cervical part of the spine; countertraction is secured by the patient's sitting against a back rest at an angle of at least 60 degrees. After reduction, of course, the traction is rapidly released, and after about four weeks a plaster cast is used.

Denis [1020] describes the use of open reduction in the treatment of irreducible dislocation of the cervical portion of the spine, using the method (similar to that described by Davis) of open reduction by direct visualization, in which the articular surfaces are levered apart and the dislocated vertebra then fastened to the adjacent intact vertebra with wire. The author even advises this method in paraplegia and cervical quadriplegia.

Ingebrigtsen [1021] discusses the same problem at some length. His experience was rather unsatisfactory, since 3 of the 4 patients operated on died. He obtained a satisfactory result in the successful case: In spite of the fact that the patient had complete paraplegia in the initial stages, he made an almost complete recovery; this case has been followed for some thirteen years. The author concludes that fractures and dislocations of the spinal column, with neurologic symptoms, including a complete transverse lesion, should be treated by immediate open reduction. In cases in which the cord has been completely crushed the operation will be of no avail, but if complete crushing has not occurred the operation may be the means for rehabilitation of the patient.

1019. Guthkelch, A. N.: Management of Recent Fracture-Dislocations of the Cervical Spine, Brit. M. J. **2**:880-881 (Dec. 22) 1945.

1020. Denis, R.: Treatment of Dislocations of the Cervical Spine by Traction, Mém. Acad. de chir. **72**:349-352 (June 19-26) 1946.

1021. Ingebrigtsen, R.: Dislocation and Fracture-Dislocation of the Spinal Column, Acta chir. Scandinav. **94**:455-469, 1946.

Boorstein [1022] discusses a series of compression fractures, basing his review on 160 cases. His is a comprehensive study, in which the degrees of compression fracture are described as mild, severe and central; cases are classified according to sex and occupation of the patient, area of the spine and nerves involved, treatment and results. Routine treatment in these cases was rest on a Bradford frame in a hyperextended position, followed by immobilization in a plaster jacket or two plaster shells and, finally, use of a spinal brace. Attention is called to the fact that full recovery may take from one to two years. The author is in agreement with Daniels [966] in stating that early operation should be performed when a dislocation is present or when a fragment of bone is pressing on the canal. However, in this series, 9 of 11 patients having laminectomy died.

In discussing the complications in the various types of fractures and fracture-dislocations with damage to the spinal cord, Christensen [1023] concludes that whenever possible an automatic bladder should be allowed to develop before the patient is catheterized. The author calls attention to the fact that this procedure has been recommended by many surgeons in the past, that there is no danger of rupture of the bladder and that the bladder empties well after use of this method for three or four days. On the other hand, repeated catheterization or the use of an indwelling catheter too frequently causes urinary infection.

Brage [1024] describes 1 case, in which he diagnosed an avulsion of the tubercle of the transverse apophysis of the first dorsal vertebra. Some confusion arose, since the symptoms were similar to scalenus anticus syndrome. The author indicates that the proper treatment in such cases is probably conservative management until the fragment can be successfully removed.

Ribo Rius [1025] describes 1 case of fractured spine due to the spasm of tetanus.

Wetzel [1026] describes 1 case of "shoveler's disease" (fracture of the dorsal spinous processes) and discusses the medicolegal aspects, particularly in regard to employee compensation.

1022. Boorstein, S. W.: Treatment of Compression Fracture of the Spine, Am. J. Surg. **71**:216-221 (Feb.) 1946.

1023. Christensen, L.: Infections of the Urinary Tract Following Spine Fractures, Ugesk. f. læger **107**:283-287 (April 5) 1945.

1024. Brage, D.: Traumatic Detachment of Transverse Apophysis of First Dorsal Vertebra, Prensa méd. argent. **33**:928-930 (May 3) 1946

1025. Ribo Rius, L.: Fracture of the Spine Due to Tetanus, Med. clin., Barcelona **6**:273-276 (April) 1946.

1026. Wetzel, E.: Shoveler's Disease Among Agricultural Workers, Schweiz. med. Wchnschr. **76**:990-991 (Sept. 28) 1946.

[ED. NOTE (W. G. S.).—None of these articles presents anything particularly new or original, but they give helpful suggestions for the treatment of these serious injuries, particularly fracture-dislocations of the cervical portion of the pine.]

INJURIES TO THE MANDIBLE AND ABOUT THE FACE

Giordanengo [1027] presents a general discussion of the causes, pathologic features, age range and diagnosis in luxation of the mandible. He describes the classic method of reduction by manipulation of the thumb within the patient's mouth.

Meade [1028] describes a case of fracture of the neck of the condyle, with displacement; treatment was by open reduction. The author describes in some detail his method of fixation with circumferential sutures, followed by fixation of the jaw with a block placed between the molar teeth and the incisors held together by rubber traction.

Clarkson, Wilson and Lawrie [1029] give a report on 1,000 cases of fracture of the mandible in which treatment was administered by a maxillofacial surgical unit of the British Army. Six hundred patients were returned to active duty. The authors stress the importance of early closure of facial wounds in order to expedite recovery and minimize scarring. They used various methods of fixation, all more or less successful, and suggested that different methods were indicated for the treatment of different conditions. Tracheotomy was necessary in 27 cases; the authors state the belief that it should be done more frequently. For grafting they recommend the use of cancellous bone rather than molded or model grafts of cortical bone.

[ED. NOTE (W. S. G.).—This is a satisfactory and comprehensive article, well worth further study.]

1027. Giordanengo, G.: Luxations of the Mandible, Minerva med. **2**:282 (Sept. 29) 1942.

1028. Meade, H. S.: Dislocation of the Mandible, Irish J. M. Sc. **2**:98-99 (March) 1946.

1029. Clarkson, P.; Wilson, T. H. H., and Lawrie, R. S.: Treatment of Jaw and Face Casualties in the British Army, Ann. Surg. **123**:190-208 (Feb.) 1946.

CORRECTION

The last sentence of the article "Precautions and Results in Gastrectomy," by Drs. Ward H. Eastman and Warren H. Cole (September issue, page 768), should read: "The highest number of deaths from any single complication occurred in leakage of the duodenal stump (3 deaths) and cardiac disease (3 deaths)."

THE RUDDOCK PERITONEOSCOPE

Peritoneoscopy is the procedure of visualizing the peritoneal cavity and its contents by means of an optical instrument. The Ruddock Peritoneoscope allows one to see, through a mere puncture, the diseased organs clearly and sharply in the peritoneal cavity without a laparotomy and with little discomfort to the patient. This procedure is especially ideal when a biopsy from tumors or tissues may be obtained after recognition of the pathology.

The development of the Ruddock Peritoneoscope was prompted by the long record of successful use of existing cystoscopes and thoracoscopes for endoscopic examination of body cavities, and for operating procedures. It follows therefore that the time proven principles and design features of our standard instruments are immediately discernible in this new peritoneoscopic equipment. The characteristics of the well-known McCarthy *Foroblique Visual System were found to ideally provide the natural telescopic picture so necessary for rapid and precise interpretation.

Departures from standard design were made whenever changes aided the specific requirements or enhanced the niceties of technique.

The illustration at the right represents a sectional view showing the technique of pelvic examinations with a view of pelvic organs obtained through peritoneoscope after pneumoperitoneum is produced. The diagram shows the manipulation of the pelvic organs through the vagina.

A booklet devoted to the Ruddock Peritoneoscope including Peritoneoscopy technique which appeared in SURGERY, GYNECOLOGY AND OBSTETRICS, November, 1937, Volume 65, 623-630, will be mailed on request.

*Foroblique is our registered trademark to designate our obliquely forward visual telescopic system.

ESTABLISHED IN 1900 BY REINHOLD H. WAPPLER

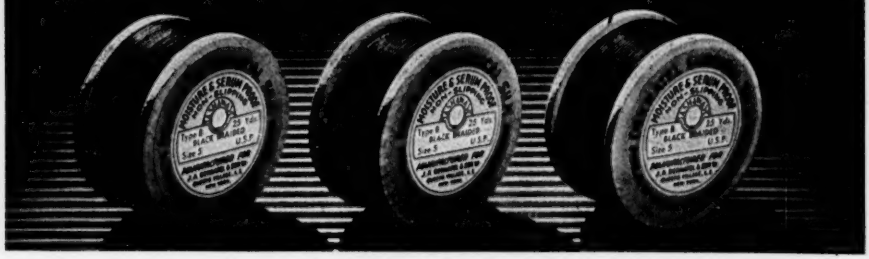
A.C.M.I. TRADE MARK

FREDERICK C. WALLACE PRESIDENT

AMERICAN CYSTOSCOPE MAKERS, INC.

1241 LEXINGTON AVE. NEW YORK 29, N. Y.

HIGH QUALITY DEKNATEL SURGICAL SUTURES



Through the years the rigidly maintained quality of Deknatel Surgical Sutures, both silk and nylon, has won ever increasing use by the medical profession. Deknatel Sutures are the original braided and treated sutures, moisture and serum resistant.

Their specially braided structure assures smooth, splinterless surface. Other proven advantages include certain and easy manipulation, soft knots and ends, superiority where wet dressings are used, extra tensile strength that permits use of smaller sizes.

SOLD BY SURGICAL—HOSPITAL SUPPLY HOUSES

J. A. DEKNATEL & SON QUEENS VILLAGE 8, LONG ISLAND, N. Y.

Health Facts

YOU WOULD GIVE PATIENTS IF TIME PERMITTED

HYGEIA

The Health Magazine

will give your patients an excellent understanding of health matters, make them intelligently health conscious, less dependent on "doctoring" themselves, more faithful in seeking your continued guidance in health and well being. Giving them HYGEIA—or introducing them to this rich source of reliable health facts, will constitute a strong "plus" value in your service to them.

MONTHLY

$3.00 a year

2 subscriptions, $5.00

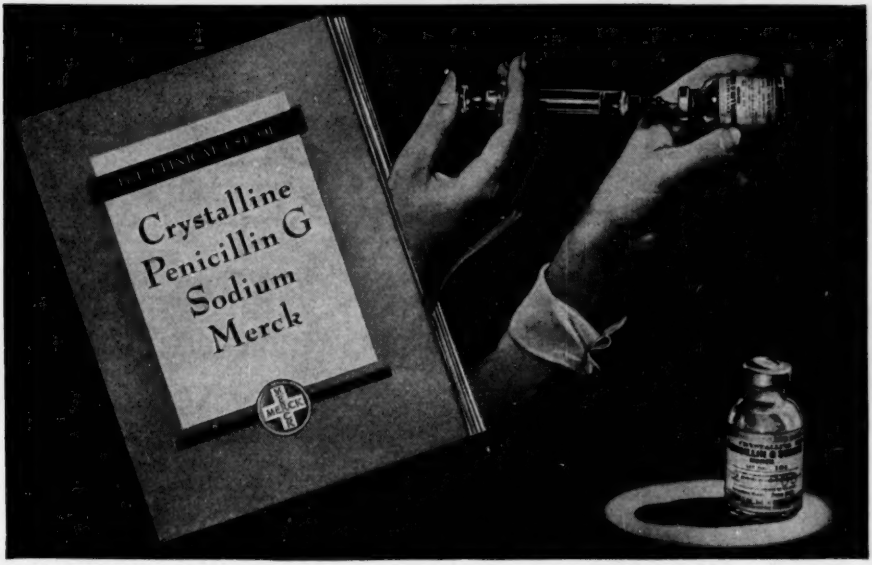
While they wait—

let patients read HYGEIA on your reception room table!

MAGAZINE OF HEALTH

AMERICAN MEDICAL ASSN.

535 North Dearborn Street • Chicago 10



This booklet will be sent on request.

4 SIGNIFICANT REASONS WHY MANY PHYSICIANS AND HOSPITALS PREFER . . .

(1) PURITY—Crystalline Penicillin G Sodium Merck is unsurpassed in purity. Removal of impurities and therapeutically inert materials, and the absence of substances which may act as foreign bodies make this form of penicillin suitable for *all* routes of administration which may be indicated, including intrathecal injection.

(2) RAPID ABSORPTION AND THERAPEUTIC EFFECT—Prompt absorption of the penicillin in aqueous solution permits rapid therapeutic action. This often is an important consideration, particularly in serious and fulminating infections.

(3) SIMPLICITY OF ADMINISTRATION—Aqueous solutions of Crystalline Penicillin G Sodium Merck are easy to handle and inject. Pain and irritation on injection are reduced to a minimum.

(4) EASY ADAPTABILITY TO THERAPY—Crystalline Penicillin G Sodium Merck never is contraindicated in cases in which penicillin itself is tolerated and indicated.

● We submit these four reasons for specifying Crystalline Penicillin G Sodium Merck when penicillin is indicated.

CRYSTALLINE PENICILLIN G SODIUM MERCK

COUNCIL ACCEPTED

MERCK & CO., Inc. *Manufacturing Chemists* RAHWAY, N. J.

AND NOW THROUGH

A New Grip on Problems of Industrial Medicine

The Forthcoming: ARCHIVES of INDUSTRIAL HYGIENE and OCCUPATIONAL MEDICINE

Inaugural Issue: January 1950.

Edited by: Men of outstanding reputation in the fields of industrial health and preventive industrial hygiene.

Prof. Philip Drinker, Boston, Chief Editor
Robert Kehoe, M.D., Cincinnati; James Sterner, M.D., Rochester, N. Y.; Frank Patty, Detroit, Mich.; Theodore Hatch, Pittsburgh; Frank Princi, M.D., Denver; Fenn E. Poole, M.D., Glendale, Calif.; William A. Sawyer, Rochester, N. Y.

Covering the RESEARCH AND FIELD ASPECTS of industrial hygiene and the CLINICAL AND MEDICAL ASPECTS of occupational industrial health programs.

Merging the best features of Occupational Medicine and The Journal of Industrial Hygiene and Toxicology.

Integrated closely with the activities of the Council of Industrial Health of the A. M. A. and the American Industrial Hygiene Association.

A BETTER AND MORE USEFUL JOURNAL of industrial medicine! Such is the result which the Editorial Board of ARCHIVES of INDUSTRIAL HYGIENE and OCCUPATIONAL MEDICINE has achieved by combining parallel publications.

To the thousands of physicians who are directly or indirectly concerned today with medicine in industry, the new journal will bring reports of the continuing and important developments in the field, with original articles covering problems and day to day experiences of physicians in industry; an excellent abstracting service similar to that carried in the Journal of Industrial Hygiene and Toxicology; additional foreign journal abstracting; reviews.

Whether servicing industrial firms, attending employees, applying to general practice some of the findings of industrial medicine, or merely *watching* this expanding field, you will want to receive this vital new periodical *from the first issue.*

AMERICAN MEDICAL ASSOCIATION
535 N. Dearborn, Chicago 10

Enter my subscription to ARCHIVES of INDUSTRIAL HYGIENE and OCCUPATIONAL MEDICINE to start *with the first issue.* Per year, $8.00 in U. S. (Canadian, $8.40; Foreign, $9.00)

I enclose check..... Please bill me.....

Name.....

Address.....

THE ARCHIVES OF SURGERY is published by the American Medical Association for the advancement of surgery and as a medium of publication for research, clinical observations and experimental work in surgery.

Manuscripts for publication and correspondence relating to the editorial management, to communications, subscriptions, reprints, etc., should be addressed, ARCHIVES OF SURGERY, American Medical Association, 535 North Dearborn Street, Chicago 10.

Articles are accepted for publication on condition that they are contributed solely to the ARCHIVES OF SURGERY. Manuscripts must be typewritten, preferably double spaced, and the original copy should be submitted. Zinc etchings and halftones will be supplied by the Association when the original illustrations warrant reproduction and when their number is not considered excessive.

Footnotes and bibliographies (the latter are used only in exhaustive reviews of the literature) should conform to the style of the *Quarterly Cumulative Index Medicus*. This requires, in the order given: name of author, title of article and name of periodical, with volume, page, month—day of month if the journal appears weekly—and year.

Matter appearing in the ARCHIVES OF SURGERY is covered by copyright, but as a rule no objection will be made to its reproduction in a reputable medical journal if proper credit is given. However, the reproduction for commercial purposes of articles appearing in the ARCHIVES OF SURGERY or in any of the other publications issued by the Association will not be permitted.

The ARCHIVES OF SURGERY is issued monthly. The annual subscription price (for tw volumes) is as follows: domestic, $10.00; Canadian, $10.40; foreign, $11.50, including postage. Single copies are $1.00, postpaid, except the August 1940 issue, which sells for $1.80.

Checks, money orders and drafts should be made payable to the American Medical Association.

OTHER PERIODICAL PUBLICATIONS
of the American Medical Association

THE JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION—Weekly. Covers all the medical sciences and matters of general medical interest. Illustrated. Annual subscription price (three volumes): domestic, $12.00; Canadian, $13.50; foreign, $16.00. Single copies, 35 cents.

ARCHIVES OF INTERNAL MEDICINE—Monthly. Devoted to the publication of advanced original clinical and laboratory investigations in internal medicine. Illustrated. Annual subscription price (two volumes): domestic, $8.00; Canadian, $8.40; foreign, $9.00. Single copies, 85 cents.

ARCHIVES OF NEUROLOGY AND PSYCHIATRY—Monthly. A medium for the presentation of original articles on nervous and mental diseases, with abstracts from foreign and domestic literature, book reviews, transactions of special societies, etc. Illustrated. Annual subscription price (two volumes): domestic, $10.00; Canadian, $10.40; foreign, $11.50. Single copies, $1.00.

ARCHIVES OF DERMATOLOGY AND SYPHILOLOGY—Monthly. Devoted to advancing the knowledge of and progress in cutaneous diseases and syphilis. Publishes original contributions and abstracts of the literature on these two subjects, transactions of the important dermatologic societies, book reviews, etc. Illustrated. Annual subscription price (two volumes): domestic, $10.00; Canadian, $10.40; foreign, $11.50. Single copies, $1.00.

AMERICAN JOURNAL OF DISEASES OF CHILDREN—Monthly. Presents pediatrics as a medical science and as a social problem. Includes carefully prepared reviews, based on recent pediatric literature, abstracts from foreign and domestic literature, book reviews, transactions of special societies, etc. Illustrated. Annual subscription price (two volumes): domestic, $10.00; Canadian, $10.40; foreign, $11.50. Single copies, $1.00.

ARCHIVES OF OPHTHALMOLOGY—Monthly. Includes original articles on diseases of the eye, abstracts from foreign and domestic literature, book reviews, transactions of special societies, etc. Illustrated. Annual subscription price (two volumes): domestic, $10.00; Canadian, $10.40; foreign, $11.00. Single copies, $1.00.

ARCHIVES OF OTOLARYNGOLOGY—Monthly. A medium for the presentation of original articles on diseases of the ear, nose and throat, with abstracts from foreign and domestic literature, book reviews, transactions of special societies, etc. Illustrated. Annual subscription price (two volumes): domestic, $10.00; Canadian, $10.40; foreign, $11.00. Single copies, $1.00.

ARCHIVES OF PATHOLOGY—Monthly. A periodical devoted to the publication of original articles and general reviews in the field of pathology. Illustrated. Annual subscription price (two volumes): domestic, $6.00; Canadian, $6.40; foreign, $7.00. Single copies, 75 cents, except special issues.

QUARTERLY CUMULATIVE INDEX MEDICUS—Quarterly. A complete subject and author index to the worth while current medical literature of the world. Issued four times a year. Second and fourth volumes bound for permanent reference. Subscription price, calendar year: domestic, $15.00; Canadian, $17.00; foreign, $17.00.

AMERICAN MEDICAL ASSOCIATION

535 North Dearborn Street **CHICAGO 10**

CONTENTS

PAGE

Acute Abdominal Manifestations in Sickle Cell Disease: A Report of Three Cases, with Laparotomy in Two. PHILIP CRASTNOPOL, M.D., AND CHARLES F. STEWART, M.D., NEW YORK 993

Echinococcal Cysts Obstructing the Common Bile Duct: Report of Case. THOMAS N. POORE, M.D.; CHARLES P. MARVIN, M.D., AND WALTMAN WALTERS, M.D., ROCHESTER, MINN. 1001

Chronic Cholecystitis Produced by Division of the Sphincter of Oddi. S. H. GRAY, M.D.; J. G. PROBSTEIN, M.D., AND LEO A. SACHAR, M.D., ST. LOUIS 1007

Threshold of Thermal Trauma and Influence of Adrenal Cortical and Posterior Pituitary Extracts on the Capillary and Chemical Changes: An Experimental Study. OLIVER COPE, M.D.; JOHN B. GRAHAM, M.D.; GEORGE MIXTER JR., M.D., AND MARGARET R. BALL, A.B., BOSTON 1015

Effect of Therapeutic Cold on the Circulation of Blood and Lymph in Thermal Burns: An Experimental Study. JOHN L. LANGOHR, M.D.; LEON ROSENFELD, M.D.; CORA R. OWEN, PH.D., AND OLIVER COPE, M.D., BOSTON 1031

Circulation of the Blood and Lymph in Frostbite and Influence of Therapeutic Cold and Warmth: An Experimental Study. LEON ROSENFELD, M.D.; JOHN L. LANGOHR, M.D.; CORA R. OWEN, PH.D., AND OLIVER COPE, M.D., BOSTON 1045

Explorations into the Psysiologic Basis for the Therapeutic Use of Restrictive Bandages in Thermal Trauma: An Experimental Study. FREDERIC W. RHINELANDER, M.D.; JOHN L. LANGOHR, M.D., AND OLIVER COPE, M.D., BOSTON 1056

Mortality and Morbidity in Surgery of the Biliary Tract: A Comparison of Two Consecutive Ten Year Periods. WILLIS G. DIFFENBAUGH, M.D., AND SELIM W. MCARTHUR, M.D., CHICAGO 1070

Abdominal Operations on Patients with Chronic Paraplegia: Report of Cases. JACK GREENFIELD, M.D., MEMPHIS, TENN. 1077

Adenomatous Goiters With and Without Hyperthyroidism: Some Aspects of the Relationship of the Microscopic Appearance to Hyperthyroidism. JAMES R. JOHNSON, M.D., ROCHESTER, MINN. 1088

Regulation of Longitudinal Bone Growth. STERLING G. PARKER, M.D., DECATUR, ILL. 1100

Ligation of the Vena Cava in Extending Thrombophlebitis. EUGENE E. CLIFFTON, M.D., NEW HAVEN, CONN., AND CAPTAIN J. C. NEEL, MEDICAL CORPS, ARMY OF THE UNITED STATES 1122

Significance of the Serosal Arterioles in Resuscitation of the Small Bowel. BERNARD J. FICARRA, M.D., BROOKLYN 1135

Progress in Orthopedic Surgery for 1946. A Review Prepared by an Editorial Board of the American Academy of Orthopaedic Surgeons:

XIX. Fractures. WALTER G. STUCK, M.D., SAN ANTONIO, TEXAS; DON H. O'DONOGHUE, M.D., AND CHARLES R. ROUNTREE, M.D., OKLAHOMA CITY; RUFUS H. ALLDREDGE, M.D., NEW ORLEANS, AND PAUL L. NORTON, M.D., BROOKLINE, MASS. 1139